OM protein - protein search, using sw model

Run on: March 28, 2005, 16:30:33 ; Search time 72 Seconds
(without alignments)
145.035 Million cell updates/sec

Title: US-09-787-082A-12
Perfect score: 150
Sequence: 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 50 summaries

Database : A_Geneseq_16Dec04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	144	96.0	27	2	AAR32779	Aar32779 GVIA omeg
2	144	96.0	27	2	AAW12969	Aaw12969 Omega con
3	144	96.0	27	3	AAY56475	Aay56475 Natural o
4	144	96.0	27	3	AAY43716	Aay43716 Amino aci
5	141	94.0	27	2	AAR39610	Aar39610 GVIA/SNX1
6	141	94.0	27	2	AAR37754	Aar37754 GVIA/SNX-
7	141	94.0	27	2	AAR76091	Aar76091 Omega con
8	141	94.0	27	2	AAW19546	Aaw19546 Natural o
9	141	94.0	27	2	AAW72607	Aaw72607 Conus gen
10	141	94.0	27	2	AAW95566	Aaw95566 Omega-con
11	141	94.0	27	2	AAY42337	Aay42337 Omega-con
12	141	94.0	27	3	AAB14354	Aab14354 Omega-con
13	141	94.0	27	4	AAB98074	Aab98074 Conotoxin
14	141	94.0	27	4	AAB19444	Aab19444 Primary s
15	141	94.0	27	5	AAO15122	Aao15122 Cone snai
16	141	94.0	73	2	AAR38796	Aar38796 Conotoxin
17	141	94.0	73	5	ABB96642	Abb96642 Omega-con
18	136	90.7	27	5	ABB96848	Abb96848 Omega-con
19	136	90.7	73	5	ABB96640	Abb96640 Omega-con
20	135	90.0	27	2	AAR51035	Aar51035 N-type ca
21	121	80.7	26	5	ABB96747	Abb96747 Omega-con
22	121	80.7	27	5	ABB96745	Abb96745 Omega-con
23	121	80.7	28	5	ABB96746	Abb96746 Omega-con
24	120	80.0	27	2	AAR32783	Aar32783 TVIA omeg
25	120	80.0	27	2	AAW12973	Aaw12973 Omega con
26	120	80.0	27	3	AAY56479	Aay56479 Natural o
27	117	78.0	27	2	AAR39614	Aar39614 TVIA/SNX1
28	117	78.0	27	2	AAR37759	Aar37759 TVIA/SNX-
29	117	78.0	27	2	AAR76095	Aar76095 Omega con
30	117	78.0	27	2	AAW19550	Aaw19550 Natural o
31	117	78.0	27	2	AAW72611	Aaw72611 Conus gen
32	117	78.0	27	2	AAW95570	Aaw95570 Omega-con
33	117	78.0	27	2	AAY42340	Aay42340 Omega-con
34	117	78.0	27	3	AAB14358	Aab14358 Omega-con
35	117	78.0	27	4	AAB19448	Aab19448 Primary s
36	117	78.0	73	5	ABB96688	Abb96688 Omega-con
37	116	77.3	27	5	ABB96743	Abb96743 Omega-con
38	115.5	77.0	24	4	AAB92218	Aab92218 Toxin pep
39	114	76.0	27	2	AAR38517	Aar38517 Omega-con
40	112	74.7	30	5	ABB96856	Abb96856 Omega-con
41	112	74.7	75	5	ABB96653	Abb96653 Omega-con
42	111	74.0	27	2	AAR12543	Aar12543 Omega con
43	109	72.7	27	2	AAW12986	Aaw12986 Omega con
44	109	72.7	27	3	AAY56497	Aay56497 Analogue
45	109	72.7	27	3	AAB14371	Aab14371 Omega-con
46	108	72.0	27	2	AAW12996	Aaw12996 Omega con
47	108	72.0	27	2	AAW72627	Aaw72627 Conus gen
48	108	72.0	27	3	AAY56498	Aay56498 Analogue
49	108	72.0	27	3	AAB14378	Aab14378 Omega-con
50	108	72.0	27	4	AAB19464	Aab19464 Sequence

ALIGNMENTS

RESULT 1
AAR32779
ID AAR32779 standard; peptide; 27 AA.
XX
AC AAR32779;
XX
DT 28-JUN-1993 (first entry)
XX
DE GVIA omega conotoxin peptide.
XX
KW OCT; neuronal damage reduction; ischemia; secondary damage; stroke.
XX
OS Synthetic.
XX
PN US5189020-A.
XX
PD 23-FEB-1993.
XX
PF 02-AUG-1990; 90US-00561766.
XX
PR 22-NOV-1989; 89US-00440094.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bitner RS, Bowersox SS, Fox JA, Valentino KL;
PI Yamashiro DH, Tsubokawa M;
XX
DR WPI; 1993-085564/10.
XX
PT Reducing neuronal damage due to ischaemia - involves using omega
PT conotoxin peptide or fragment.
XX
PS Disclosure; Fig 1; 32pp; English.
XX
CC The sequence is that of the GVIA omega conotoxin (OCT) peptide which can
CC bind to an OCT binding protein, inhibit voltage-gated calcium currents
CC selectively in neuronal tissue and inhibit neuronal transmitter release
CC selectively in neuronal tissue. These properties all occur within the
CC range of those of MVIIB, GVIIA, RVIA, or pref. MVIIA and GVIA OCTs. The
CC peptide can be used in reducing or preventing both anatomical and
CC functional secondary damage related to ischemia, generally as associated
CC with stroke
XX

SQ Sequence 27 AA;

Query Match 96.0%; Score 144; DB 2; Length 27;
Best Local Similarity 100.0%; Pred. No. 5e-10;
Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
Db 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27

RESULT 2
AAW12969
ID AAW12969 standard; peptide; 27 AA.
XX
AC AAW12969;
XX
DT 25-MAR-2003 (revised)
DT 22-APR-1997 (first entry)
XX
DE Omega conopeptide SNX-124.
XX
KW Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW acute dystonic reactions; inflammation; epilepsy.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Modified-site 4
FT /label= Hyp
FT Modified-site 10
FT /label= Hyp
FT Modified-site 21
FT /label= Hyp
XX
PN US5587454-A.
XX
PD 24-DEC-1996.
XX
PF 15-APR-1993; 93US-00049794.
XX
PR 30-DEC-1991; 91US-00814759.
PR 30-DEC-1992; 92WO-US011349.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Gohil KC, Miljanich GP, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1997-064830/06.
XX
PT Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT neuropathic pain.
XX
PS Disclosure; Col 41-42; 58pp; English.
XX
CC The present peptide is an omega conopeptide, useful as an analgesic,
CC especially for treating neuropathic pain. The peptide, which can be
CC prepared by solid phase synthesis, can also be used to inhibit neuronal
CC damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC reactions, inflammation and epilepsy. (Updated on 25-MAR-2003 to correct
CC PF field.)
XX
SQ Sequence 27 AA;

Query Match 96.0%; Score 144; DB 2; Length 27;
Best Local Similarity 100.0%; Pred. No. 5e-10;
Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
Db 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27

RESULT 3
AAY56475
ID AAY56475 standard; peptide; 27 AA.
XX
AC AAY56475;
XX
DT 16-FEB-2000 (first entry)
XX
DE Natural omega conopeptide GVIA/SNX-124.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Misc-difference 4
FT /note= "unspecified"
FT Misc-difference 10
FT /note= "unspecified"
FT Misc-difference 21
FT /note= "unspecified"
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 1; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 27 AA;

Query Match 96.0%; Score 144; DB 3; Length 27;
Best Local Similarity 100.0%; Pred. No. 5e-10;
Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
Db 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27

```
RESULT 4
AAY43716
ID   AAY43716 standard; peptide; 27 AA.
XX
AC   AAY43716;
XX
DT   11-FEB-2000  (first entry)
XX
DE   Amino acid sequence of an omega-conotoxin GVIA.
XX
KW   Omega-conotoxin; venom; predatory marine snail; N-type calcium channel;
KW   neuronal damage reduction; ischemia; analgesia; opiate analgesia;
KW   schizophrenia; stimulant induced psychosis; hypertension; inflammation;
KW   bronchotension; neuropathic pain; voltage sensitive calcium channel.
XX
OS   Conus geographus.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Hyp
FT                   /note= "4-hydroxy proline"
FT   Modified-site   10
FT                   /label= Hyp
FT                   /note= "4-hydroxy proline"
FT   Modified-site   21
FT                   /label= Hyp
FT                   /note= "4-hydroxy proline"
XX
PN   WO9954350-A1.
XX
PD   28-OCT-1999.
XX
PF   16-APR-1999;   99WO-AU000288.
XX
PR   16-APR-1998;   98AU-00002989.
PR   01-FEB-1999;   99AU-00008419.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Drinkwater RD,  Lewis RJ,  Alewood PF,  Nielsen KJ;
XX
DR   WPI; 2000-013226/01.
XX
PT   Novel peptides used for the treatment of disorders and diseases where
PT   blockage of the N-type calcium channels is required.
XX
PS   Disclosure; Page 13; 81pp; English.
XX
CC   The present sequence represents an omega-conotoxin. Omega-conotoxins are
CC   isolated from venoms of predatory marine snails, and have a selectivity
CC   for N-type calcium channels over P/Q type channels, and so block N-type
CC   calcium channels. The omega-conotoxins of the invention can be used in
CC   any disease or disorder where blockage of N-type calcium channels is
CC   required, e.g. in the reduction of neuronal damage following ischemia,
CC   production of analgesia, or enhancement of opiate analgesia, in the
CC   treatment of schizophrenia, stimulant induced psychoses, hypertension,
CC   inflammation, and diseases which cause bronchotension, and also in the
CC   inhibition of progression of neuropathic pain. They can also be used in a
CC   screen to identify compounds with activity at N-type voltage sensitive
CC   calcium channels
XX
SQ   Sequence 27 AA;

  Query Match             96.0%;  Score 144;  DB 3;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 5e-10;
  Matches   27;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||||||||||||||||||||||||||||
Db          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
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RESULT 5
AAR39610
ID   AAR39610 standard; peptide; 27 AA.
XX
AC   AAR39610;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   GVIA/SNX124.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /note= "4Hyp"
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /note= "4Hyp"
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /note= "4Hyp"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 1; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27
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RESULT 6

```
AAR37754
ID   AAR37754 standard; peptide; 27 AA.
XX
AC   AAR37754;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   GVIA/SNX-124.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /note= "hydroxyproline"
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 1; 103pp; English.
XX
CC   Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC   hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC   omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC   at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC   that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC   or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC   damage caused by stroke. By delaying admin. for some time (compare
CC   US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC   greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC   intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC   be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC   in blood pressure caused by (I)). (I) is also at least as effective as
CC   the specified conotoxins for (1) selective inhibition of N-type voltage-
CC   gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC   channel mediated neurotransmitter release in neuronal tissue. Primary
CC   sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC   omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC   correct PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 7
AAR76091
ID   AAR76091 standard; peptide; 27 AA.
XX
AC   AAR76091;
XX
DT   27-AUG-2003  (revised)
DT   25-MAR-2003  (revised)
DT   02-FEB-1996  (first entry)
XX
DE   Omega conotoxin GVIA peptide.
XX
KW   Omega conotoxin; marine snail; Conus; voltage-gated Ca channel blocker;
KW   synaptosome; membrane; fish electric organ; mammalian brain; ischaemia;
KW   binding protein; binding affinity; stroke.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4-Hyp
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= 4-Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4-Hyp
FT   Modified-site   27
FT                   /note= "amidated C-terminus"
XX
PN   US5424218-A.
XX
PD   13-JUN-1995.
XX
PF   04-NOV-1993;   93US-00147714.
XX
PR   22-NOV-1989;   89US-00440094.
PR   02-AUG-1990;   90US-00561766.
PR   23-MAR-1992;   92US-00855269.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Valentino KL,  Bowersox SS,  Bitner RS,  Miljanich GP,  Yamashiro DH;
PI   Fox JA;
XX
DR   WPI; 1995-223694/29.
XX
PT   Identifying cpds. able to reduce neuronal damage caused by ischaemia - by
PT   measuring their affinity to omega conotoxin MVIIA binding site and
PT   ability e.g. to inhibit voltage gated calcium channels.
XX
PS   Disclosure; Fig 1; 31pp; English.
XX
CC   The peptides AAR76089-95 are naturally occuring omega conotoxin (OCT)
CC   peptides derived from marine snails of the Conus genus. The peptide
CC   sequences were used to chemically synthesise the OCT peptide fragments
CC   AAR76096-R76109. The OCT peptides act as voltage-gated Ca channel
CC   blockers by binding to a 210 kD protein from synaptosomal membrane
CC   preparations from fish electric organ or mammalian brains. The peptides
CC   and their synthesised fragments can be used to screen for compounds that
CC   bind to the OCT binding protein, by displacing a high affinity labelled
CC   OCT, such as MVIIA, from a synaptosomal membrane preparation. The
CC   compounds should have binding affinities and activities at least equal to
CC   those of the natural peptides (Ki 0.44-324 nM). The screened compounds
CC   are potentially useful in treating ischaemic conditions, esp. stroke, and
CC   can reduce sec. anatomical and functional damage associated with those
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CC   conditions. (Updated on 25-MAR-2003 to correct PF field.) (Updated on 27-
CC   AUG-2003 to correct OS field.)
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 8
AAW19546
ID   AAW19546 standard; peptide; 27 AA.
XX
AC   AAW19546;
XX
DT   27-AUG-2003  (revised)
DT   10-OCT-1997  (first entry)
XX
DE   Natural omega-conopeptide GVIA/SNX-124 used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /label= 4Hyp
FT   Misc-difference 10
FT                   /label= 4Hyp
FT   Misc-difference 21
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XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Disclosure; Fig 1; 47pp; English.
XX
CC   AAW19544-W19553 are naturally occurring omega conopeptides (OCs) isolated
CC   from Conus sp. (cone snails). The peptides and their analogues are used
CC   as analgesics acting by blocking N-type voltage-sensitive calcium
CC   channels. The OCs can be used to treat neuropathic pain as a result of
CC   e.g. insult to the spinal cord or peripheral nerves, cancer, bone
CC   degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes zoster
CC   neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage. (Updated on 27-AUG-2003 to
CC   correct OS field.)
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 9
AAW72607
ID   AAW72607 standard; peptide; 27 AA.
XX
AC   AAW72607;
XX
DT   27-AUG-2003  (revised)
DT   06-JAN-1999  (first entry)
XX
DE   Conus genus natural omega-conopeptide GVIA/SNX-124.
XX
KW   Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW   nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW   inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
KW   rheumatoid arthritis; epilepsy.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   10
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   21
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
XX
PN   US5824645-A.
XX
PD   20-OCT-1998.
XX
PF   01-NOV-1996;   96US-00742774.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Valentino KL,  Gohil KC,  Justice A,  Singh T;
XX
DR   WPI; 1998-582596/49.
XX
PT   Treatment of inflammation, comprises administration of omega-conopeptide
PT   - effective to block voltage-gated calcium channels, bind with high
PT   affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT   release.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   A method has been developed for the treatment of inflammation in a
CC   subject. The method comprises administration of an omega-conopeptide
CC   effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC   high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC   neurotransmitter release from nervous tissue. The method is used to treat
CC   inflammation and associated pain. The treatment can also be used to
CC   produce analgesia (especially in subjects experiencing neuropathic pain);
```

```
CC   and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC   reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC   represents a natural omega-conopeptide. Omega-conopeptides are components
CC   of peptide toxins produced by marine snails of the genus Conus, and which
CC   act as calcium channel blockers. (Updated on 27-AUG-2003 to correct OS
CC   field.)
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 10
AAW95566
ID   AAW95566 standard; protein; 27 AA.
XX
AC   AAW95566;
XX
DT   29-MAR-1999  (first entry)
XX
DE   Omega-conopeptide GVIA/SNX-124.
XX
KW   Omega-conopeptide; peptide toxin; snail; calcium channel blocker;
KW   analgesia; guinea pig ileum; omega-conotoxin; pain; neuropathic.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   10
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   21
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   27
FT                   /note= "C-terminal amide"
XX
PN   US5859186-A.
XX
PD   12-JAN-1999.
XX
PF   03-JUL-1996;   96US-00675354.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Gohil KC,  Valentino KL,  Justice A,  Singh T;
XX
DR   WPI; 1999-120002/10.
XX
PT   Production of analgesia in mammal - by administration of omega cono-
PT   peptide(s).
XX
PS   Disclosure; Fig 1A; 59pp; English.
XX
CC   Sequences AAW95564-573 represent primary sequences of natural omega-
CC   conopeptides. Omega-conopeptides are components of peptide toxins
CC   produced by marine snails of the genus Conus, and which act as calcium
CC   channel blockers. The invention relates to a method of producing
CC   analgesia in a mammal that comprises administering an omega conopeptide
CC   having activities in (a) inhibiting electrically stimulated contraction
CC   of guinea pig ileum and (b) selectively binding to omega conopeptide
CC   MVIIA binding sites in neuronal tissue, where these activities are within
CC   the ranges of those of omega-conotoxins MVIIA and TVIA. The method is
CC   used for treating chronic pain, especially neuropathic pain
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 11
AAY42337
ID   AAY42337 standard; peptide; 27 AA.
XX
AC   AAY42337;
XX
DT   20-DEC-1999  (first entry)
XX
DE   Omega-conotoxin OCT GVIA.
XX
KW   Calcium channel; neuron; retina; optic nerve; trauma; ischaemia; vision;
KW   prevention.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4Hyp
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= 4Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4Hyp
FT   Misc-difference 25
FT                   /note= "Optionally contains C-terminal amide"
XX
PN   US5965534-A.
XX
PD   12-OCT-1999.
XX
PF   13-MAR-1998;   98US-00039168.
XX
PR   22-NOV-1995;   95US-00562142.
XX
PA   (ALCO-) ALCON LAB INC.
XX
PI   Hellberg M,  Pang I,  Kapin M;
XX
DR   WPI; 1999-579926/49.
XX
PT   Treatment or prevention of retinal or optic nerve head damage comprises
PT   administration of an omega-conotoxin derivative.
XX
PS   Claim 2; Col 9-10; 7pp; English.
XX
CC   This sequence represents omega-conotoxin OCT GVIA. Omega-conotoxins
CC   selectively block N-type calcium channels responsible for calcium influx
CC   in neurons. Acute retinal or optic nerve damage, which can result in the
CC   loss of vision, is caused by acute trauma and pathological events such as
CC   ischaemia, hypoxia or oedema. The release of excitatory amino acids is
CC   implicated in ischaemia-related neuronal and retinal damage, with
CC   excitatory amino acid release leading to excessive stimulation of post-
CC   synaptic excitatory amino acid receptors, which can result in cell
CC   injury. The release of such excitatory amino acids from presynaptic nerve
CC   terminals is dependent upon an elevation of calcium in the nerve
```

CC terminal. This presynaptic calcium influx is mediated by the N-type
CC calcium channels that are inhibited by omega-conotoxins. Intraocular
CC administration of at least one omega-conotoxin could be used for the
CC treatment or prevention of retinal or optic nerve head damage resulting
CC from acute traumatic or acute ischaemic events
XX
SQ Sequence 27 AA;

Query Match 94.0%; Score 141; DB 2; Length 27;
Best Local Similarity 88.9%; Pred. No. 1.1e-09;
Matches 24; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
||| ||||| |||||||||| ||||||
Db 1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27

RESULT 12
AAB14354
ID AAB14354 standard; peptide; 27 AA.
XX
AC AAB14354;
XX
DT 06-DEC-2000 (first entry)
XX
DE Omega-conopeptide GVIA/SNX-124.
XX
KW Marine snail; omega-conopeptide; calcium channel blocker; GVIA; SNX-124;
KW toxin; analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW acute dystonic reaction; inflammation; epilepsy.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Modified-site 4
FT /label= 4Hyp
FT Disulfide-bond 8. .19
FT Modified-site 10
FT /label= 4Hyp
FT Disulfide-bond 15. .26
FT Modified-site 21
FT /label= 4Hyp
FT Modified-site 27
FT /note= "C-terminal amide"
XX
PN US6087091-A.
XX
PD 11-JUL-2000.
XX
PF 23-APR-1999; 99US-00298017.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2000-490177/43.
XX
PT Selecting a compound for producing analgesia involves measuring activity
PT of test compound in blocking voltage-gated calcium channels, binding to
PT omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS Disclosure; Fig 1; 58pp; English.
XX
CC The present sequence is an omega-conopeptide from marine snails of the
CC genus Conus. Omega-conopeptides are components of peptide toxins produced
CC by the cone snails, and which act as calcium channel blockers. Natural
CC omega-conopeptides and their derivatives may be useful for producing
CC analgesia in nociceptive and neuropathic pain. The peptides bind to omega
CC -conopeptide binding sites, which are present mainly in neuronal tissue,
CC and inhibit norepinephrine release from nervous tissue. Conopeptides such
CC as MVIIA and TVIA are effective as therapeutic agents for treating
CC neurogenic conditions such as schizophrenia, tardive dyskinesia and acute
CC dystonic reactions, inflammation and epilepsy
XX
SQ Sequence 27 AA;

Query Match 94.0%; Score 141; DB 3; Length 27;
Best Local Similarity 88.9%; Pred. No. 1.1e-09;
Matches 24; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
||| ||||| |||||||||| ||||||
Db 1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27

RESULT 13
AAB98074
ID AAB98074 standard; peptide; 27 AA.
XX
AC AAB98074;
XX
DT 16-AUG-2001 (first entry)
XX
DE Conotoxin GVIA peptide SEQ ID NO:3.
XX
KW Mouse; N-calcium channel alpha 1B subunit; blood pressure control;
KW N-calcium channel knockout animal; blood glucose level control;
KW pain transfer; hypotensive; analgesic.
XX
OS Conus geographus.
XX
FH Key Location/Qualifiers
FT Modified-site 4
FT /note= "hydroxyproline"
FT Modified-site 10
FT /note= "hydroxyproline"
FT Modified-site 21
FT /note= "hydroxyproline"
XX
PN WO200130137-A1.
XX
PD 03-MAY-2001.
XX
PF 26-OCT-2000; 2000WO-JP007503.
XX
PR 26-OCT-1999; 99JP-00303809.
PR 16-FEB-2000; 2000JP-00037839.
PR 31-AUG-2000; 2000JP-00261979.
XX
PA (EISA) EISAI CO LTD.
XX
PI Ino M, Miyamoto N, Takahashi E, Oki T, Yoshinaga T, Hatakeyama S;
PI Niidome T, Sawada K, Nishizawa Y, Tanaka I;
XX
DR WPI; 2001-300406/31.
XX
PT N-type calcium channel deficient non-human animals useful for screening
PT for new drugs.
XX
PS Disclosure; Page 56; 64pp; Japanese.
XX
CC The present invention describes an N-type calcium channel deficient non-
CC human animal whose gene for the calcium channel has been disrupted. The
CC gene that is disrupted encodes the N-type calcium channel alpha 1B
CC subunit. Also described are: (1) a method for assaying usefulness of
CC substances using the animal; (2) a method for screening for substances
CC with potential pharmacological use; (3) useful substances found by the
CC method; and (4) a method for producing pharmaceuticals using this method

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CC   (specifically methods for producing a hypotensive drug, a pain killer and
CC   a drug for lowering blood sugar and the substances themselves). The N-
CC   type calcium channel deficient non-human animal can be used for screening
CC   substances for pharmaceutical use. Active substances include a
CC   hypotensive drug, a pain killer and a drug for lowering blood sugar. The
CC   present sequence represents the Conus geographus conotoxin GVIA peptide
CC   which is given in the exemplification of the present invention
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 4;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 14
AAB19444
ID   AAB19444 standard; peptide; 27 AA.
XX
AC   AAB19444;
XX
DT   06-MAR-2001  (first entry)
XX
DE   Primary sequence of a natural omega-conopeptide GVIA/SNX-124.
XX
KW   Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW   peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW   schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW   epilepsy.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   27
FT                   /note= "amidated C-terminal"
XX
PN   US6136786-A.
XX
PD   24-OCT-2000.
XX
PF   09-SEP-1999;   99US-00392979.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   23-JUN-1993;   93US-00081863.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
PR   23-APR-1999;   99US-00298017.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2001-030946/04.
XX
PT   Enhancing analgesia produced by opiates by administering an omega-
PT   conopeptide that inhibits electrically stimulated contraction of guinea
PT   pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT   tissues.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   The present sequence represents an omega-conopeptide. Omega-conopeptides
CC   are components of peptide toxins which act as voltage-gated calcium
CC   channel inhibitors. The peptides are used to enhance the analgesic effect
CC   produced by an opiate in a mammalian subject. The method comprises
CC   administering to the subject an omega-conopeptide which is able to
CC   inhibit electrically stimulated contraction of the guinea pig ileum and
CC   bind to omega-conopeptide MVIIA binding sites present in neuronal tissue.
CC   Omega-conopeptides are useful for enhancing the analgesic effect produced
CC   by an opiate. Omega-conopeptides may also be used in the treatment of
CC   pain, in reducing neuronal damage related to an ischemic condition in
CC   mammals, and in treating schizophrenia, tardive dyskinesia and acute
CC   dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 4;  Length 27;
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 15
AAO15122
ID   AAO15122 standard; peptide; 27 AA.
XX
AC   AAO15122;
XX
DT   22-AUG-2002  (first entry)
XX
DE   Cone snail w-conotoxin peptide GVIA.
XX
KW   Cone snail; venomous saliva; calcium channel blocking activity;
KW   stenocardia; hypertension; myocarditis; arrhythmia; cerebral ischaemia;
KW   w-conotoxin.
XX
OS   Conus sp.
XX
PN   JP2002080499-A.
XX
PD   19-MAR-2002.
XX
PF   01-SEP-2000; 2000JP-00266187.
XX
PR   01-SEP-2000; 2000JP-00266187.
XX
PA   (SUNR ) SUNTORY LTD.
XX
DR   WPI; 2002-421068/45.
XX
PT   A new peptide derived from venomous saliva of assassin bug, has calcium
PT   channel blocking activity.
XX
PS   Disclosure; Page 4; 26pp; Japanese.
XX
CC   The invention comprises peptides having calcium channel blocking
CC   activities which are derived from the venomous saliva of assassin bugs.
CC   The calcium channel blocking peptides of the invention are useful for
CC   treating stenocardia, hypertension, myocarditis, arrhythmia and cerebral
CC   ischaemia. The present amino acid sequence represents a cone snail w-
CC   conotoxin peptide
XX
SQ   Sequence 27 AA;

  Query Match             94.0%;  Score 141;  DB 5;  Length 27;
```

```
  Best Local Similarity   88.9%;  Pred. No. 1.1e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 16
AAR38796
ID   AAR38796 standard; peptide; 73 AA.
XX
AC   AAR38796;
XX
DT   22-FEB-1994  (first entry)
XX
DE   Conotoxin prepropeptide GVIA.
XX
KW   Calcium channel; four loop; toxin; MVIIB; Conus magus; GVIA; neurone;
KW   C. geographus; conotoxin; presynaptic; specificity; calcium target;
KW   cysteine; omega; framework; template domain.
XX
OS   Conus geographus.
XX
FH   Key             Location/Qualifiers
FT   Region          46. .72
FT                   /note= "Mature omega-toxin"
XX
PN   US5231011-A.
XX
PD   27-JUL-1993.
XX
PF   18-APR-1991;   91US-00689693.
XX
PR   18-APR-1991;   91US-00689693.
XX
PA   (UTAH ) UNIV UTAH.
XX
PI   Hillyard DR,  Olivera BM;
XX
DR   WPI; 1993-249725/31.
XX
PT   Formation of cysteine-rich peptide of specified di:sulphide bonding -
PT   involves forming pre:pro-peptide with N-terminal excised region which
PT   acts as templates for directing di:sulphide bond formation in cysteine-
PT   rich peptide.
XX
PS   Example 1; Col 8; 15pp; English.
XX
CC   The sequences given in AAR38795-96 represent two examples of calcium
CC   channel four loop toxins. They are MVIIB from Conus magus and GVIA from
CC   C. geographus. These conotoxins target presynaptic calcium channels and
CC   have largely overlapping specificities for different calcium targets in
CC   neuronal tissue preparations. These peptides form a four loop folded
CC   toxin molecule with a specific arrangement of cysteines referred to as
CC   the omega pattern. The cysteine framework of these two peptides differs
CC   only in the exact amino acid spacing of the two carboxy terminal inter-
CC   Cys domains. Beyond the similarity of the framework the two peptides are
CC   remarkably divergent. Only nine of the 21 non-Cys amino acids of the
CC   omega-GVIA are conserved in the omega-MVIIA. MVIIB and GVIA template
CC   domains are each 45 amino acids in length. They also show a >90%
CC   conservation of amino acid sequence with only 4 positions of amino acid
CC   non-identity. These two sequences illustrate the existence of two highly
CC   conserved template domains associated with two structurally dissimilar
CC   toxins
XX
SQ   Sequence 73 AA;

  Query Match             94.0%;  Score 141;  DB 2;  Length 73;
  Best Local Similarity   88.9%;  Pred. No. 2.6e-09;
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db         46 CKSPGSSCSPTSYNCCRSCNPYTKRCY 72


RESULT 17
ABB96642
ID   ABB96642 standard; peptide; 73 AA.
XX
AC   ABB96642;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide w-GVIA propeptide.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
DR   N-PSDB; ABL98901.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Claim 1(c); Page 44; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96595-ABB96697 represent omega-conopeptide
CC   propeptide sequences
XX
SQ   Sequence 73 AA;

  Query Match             94.0%;  Score 141;  DB 5;  Length 73;
  Best Local Similarity   88.9%;  Pred. No. 2.6e-09;
```

```
  Matches   24;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| ||||||
Db         46 CKSPGSSCSPTSYNCCRSCNPYTKRCY 72


RESULT 18
ABB96848
ID   ABB96848 standard; peptide; 27 AA.
XX
AC   ABB96848;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide G6.1 toxin sequence.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Claim 1(a); Page 71; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96807-ABB96905 represent omega-conopeptide
CC   toxin sequences
XX
SQ   Sequence 27 AA;

  Query Match             90.7%;  Score 136;  DB 5;  Length 27;
  Best Local Similarity   85.2%;  Pred. No. 4.3e-09;
  Matches   23;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| | ||||
Db          1 CKSPGSSCSPTSYNCCRSCNPYAKRCY 27


RESULT 19
ABB96640
ID   ABB96640 standard; peptide; 73 AA.
XX
AC   ABB96640;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide G6.1 propeptide.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
DR   N-PSDB; ABL98899.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Claim 1(c); Page 43; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96595-ABB96697 represent omega-conopeptide
CC   propeptide sequences
```

```
XX
SQ   Sequence 73 AA;

  Query Match             90.7%;  Score 136;  DB 5;  Length 73;
  Best Local Similarity   85.2%;  Pred. No. 1e-08;
  Matches   23;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              ||| ||||| |||||||||| | ||||
Db         46 CKSPGSSCSPTSYNCCRSCNPYAKRCY 72


RESULT 20
AAR51035
ID   AAR51035 standard; peptide; 27 AA.
XX
AC   AAR51035;
XX
DT   24-NOV-1994  (first entry)
XX
DE   N-type calcium channel affinity peptide.
XX
KW   Affinity; N-type; calcium channel; isolation; purification.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4Hyp
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= 4Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4Hyp
FT   Modified-site   27
FT                   /note= "Amidated C-terminal"
XX
PN   JP06080696-A.
XX
PD   22-MAR-1994.
XX
PF   01-SEP-1992;   92JP-00255424.
XX
PR   01-SEP-1992;   92JP-00255424.
XX
PA   (MITU ) MITSUBISHI KASEI CORP.
XX
DR   WPI; 1994-132043/16.
XX
PT   Peptide with affinity for N-type calcium channel - useful as agent for
PT   isolation and purification of calcium channel.
XX
PS   Claim 1; Page 2; 4pp; Japanese.
XX
CC   This sequence represents a peptide which has affinity for an N-type
CC   calcium channel. This peptide is preferably prepared by standard solid-
CC   phase synthesis techniques and is useful as an agent for isolation and
CC   purification of the calcium channel
XX
SQ   Sequence 27 AA;

  Query Match             90.0%;  Score 135;  DB 2;  Length 27;
  Best Local Similarity   85.2%;  Pred. No. 5.7e-09;
  Matches   23;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
              | | ||||| |||||||||| ||||||
Db          1 CASPGSSCSPTSYNCCRSCNPYTKRCY 27


RESULT 21
ABB96747
ID   ABB96747 standard; peptide; 26 AA.
XX
AC   ABB96747;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide w-GVIC generic toxin sequence.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 10
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 13
FT                   /label= OTHER
FT                   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT   Misc-difference 21
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 22
FT                   /label= OTHER
FT                   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Example 2; Page 44; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
```

```
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96698-ABB96806 represent omega-conopeptide
CC   generic toxin sequences
XX
SQ   Sequence 26 AA;

  Query Match             80.7%;  Score 121;  DB 5;  Length 26;
  Best Local Similarity   92.3%;  Pred. No. 2.4e-07;
  Matches   24;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              |||||||||||| |||||||| ||||
Db          1 CKSXGSSCSXTSXNCCRSCNXXTKRC 26


RESULT 22
ABB96745
ID   ABB96745 standard; peptide; 27 AA.
XX
AC   ABB96745;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide w-GVIA generic toxin sequence.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 10
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 13
FT                   /label= OTHER
FT                   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT   Misc-difference 21
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 22
FT                   /label= OTHER
FT                   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT   Misc-difference 27
FT                   /label= OTHER
FT                   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Example 2; Page 44; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96698-ABB96806 represent omega-conopeptide
CC   generic toxin sequences
XX
SQ   Sequence 27 AA;

  Query Match             80.7%;  Score 121;  DB 5;  Length 27;
  Best Local Similarity   92.3%;  Pred. No. 2.5e-07;
  Matches   24;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              |||||||||||| |||||||| ||||
Db          1 CKSXGSSCSXTSXNCCRSCNXXTKRC 26


RESULT 23
ABB96746
ID   ABB96746 standard; peptide; 28 AA.
XX
AC   ABB96746;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide w-GVIB generic toxin sequence.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus geographus.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /label= OTHER
FT                   /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 10
FT                   /label= OTHER
```

```
FT                  /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 13
FT                  /label= OTHER
FT                  /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                  Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT   Misc-difference 21
FT                  /label= OTHER
FT                  /note= "OTHER is Pro or Hydroxy Pro"
FT   Misc-difference 22
FT                  /label= OTHER
FT                  /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                  Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT   Misc-difference 27
FT                  /label= OTHER
FT                  /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT                  Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Example 2; Page 44; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96698-ABB96806 represent omega-conopeptide
CC   generic toxin sequences
XX
SQ   Sequence 28 AA;

  Query Match             80.7%;  Score 121;  DB 5;  Length 28;
  Best Local Similarity   92.3%;  Pred. No. 2.5e-07;
  Matches   24;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              |||||||||||| |||||||| ||||
Db          1 CKSXGSSCSXTSXNCCRSCNXXTKRC 26


RESULT 24
AAR32783
ID   AAR32783 standard; peptide; 27 AA.
XX
AC   AAR32783;
XX
DT   28-JUN-1993  (first entry)
XX
DE   TVIA omega conotoxin peptide.
XX
KW   OCT; neuronal damage reduction; ischemia; secondary damage; stroke.
XX
OS   Synthetic.
XX
PN   US5189020-A.
XX
PD   23-FEB-1993.
XX
PF   02-AUG-1990;   90US-00561766.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH,  Tsubokawa M;
XX
DR   WPI; 1993-085564/10.
XX
PT   Reducing neuronal damage due to ischaemia - involves using omega
PT   conotoxin peptide or fragment.
XX
PS   Disclosure; Fig 1; 32pp; English.
XX
CC   The sequence is that of the TVIA omega conotoxin (OCT) peptide which can
CC   bind to an OCT binding protein, inhibit voltage-gated calcium currents
CC   selectively in neuronal tissue and inhibit neuronal transmitter release
CC   selectively in neuronal tissue. These properties all occur within the
CC   range of those of MVIIB, GVIIA, RVIA, or pref. MVIIA and GVIA OCTs. The
CC   peptide can be used in reducing or preventing both anatomical and
CC   functional secondary damage related to ischemia, generally as associated
CC   with stroke
XX
SQ   Sequence 27 AA;

  Query Match             80.0%;  Score 120;  DB 2;  Length 27;
  Best Local Similarity   84.6%;  Pred. No. 3.2e-07;
  Matches   22;  Conservative    3;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | ||||||||||||||||||||:::|
Db          1 CLSXGSSCSXTSYNCCRSCNXYSRKC 26


RESULT 25
AAW12973
ID   AAW12973 standard; peptide; 27 AA.
XX
AC   AAW12973;
XX
DT   25-MAR-2003  (revised)
DT   22-APR-1997  (first entry)
XX
DE   Omega conopeptide SNX-185.
XX
KW   Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW   neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW   acute dystonic reactions; inflammation; epilepsy.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Hyp
FT   Modified-site   10
FT                   /label= Hyp
```

FT Modified-site 21
FT /label= Hyp
XX
PN US5587454-A.
XX
PD 24-DEC-1996.
XX
PF 15-APR-1993; 93US-00049794.
XX
PR 30-DEC-1991; 91US-00814759.
PR 30-DEC-1992; 92WO-US011349.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Gohil KC, Miljanich GP, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1997-064830/06.
XX
PT Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT neuropathic pain.
XX
PS Disclosure; Col 45-46; 58pp; English.
XX
CC The present peptide is an omega conopeptide, useful as an analgesic,
CC especially for treating neuropathic pain. The peptide, which can be
CC prepared by solid phase synthesis, can also be used to inhibit neuronal
CC damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC reactions, inflammation and epilepsy. In a rat paw formalin test, the
CC peptide had an ED50 of 0.043 microg in phase 1, and 0.041 microg in phase
CC 2 (by intrathecal administration). (Updated on 25-MAR-2003 to correct PF
CC field.)
XX
SQ Sequence 27 AA;

Query Match 80.0%; Score 120; DB 2; Length 27;
Best Local Similarity 84.6%; Pred. No. 3.2e-07;
Matches 22; Conservative 3; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| ||||||||||||||||||||:::|
Db 1 CLSXGSSCSXTSYNCCRSCNXYSRKC 26

RESULT 26
AAY56479
ID AAY56479 standard; peptide; 27 AA.
XX
AC AAY56479;
XX
DT 16-FEB-2000 (first entry)
XX
DE Natural omega conopeptide TVIA/SNX-185.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Misc-difference 4
FT /note= "unspecified"
FT Misc-difference 10
FT /note= "unspecified"
FT Misc-difference 21
FT /note= "unspecified"
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 1; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 27 AA;

Query Match 80.0%; Score 120; DB 3; Length 27;
Best Local Similarity 84.6%; Pred. No. 3.2e-07;
Matches 22; Conservative 3; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| ||||||||||||||||||||:::|
Db 1 CLSXGSSCSXTSYNCCRSCNXYSRKC 26

RESULT 27
AAR39614
ID AAR39614 standard; peptide; 27 AA.
XX
AC AAR39614;
XX
DT 25-MAR-2003 (revised)
DT 20-DEC-1993 (first entry)
XX
DE TVIA/SNX185.
XX
KW Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW narcotics.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Modified-site 4
FT /note= "4Hyp"
FT Disulfide-bond 8. .19
FT Modified-site 10
FT /note= "4Hyp"
FT Disulfide-bond 15. .26
FT Modified-site 21
FT /note= "4Hyp"
XX
PN WO9313128-A1.

XX
PD 08-JUL-1993.
XX
PF 30-DEC-1992; 92WO-US011349.
XX
PR 30-DEC-1991; 91US-00814759.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Justice A, Singh T, Gohil K, Valentino KL, Miljanich GP;
XX
DR WPI; 1993-227270/28.
XX
PT Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT pain etc.
XX
PS Claim 1; Fig 1; 90pp; English.
XX
CC The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC derivatives of these, which may be used to produce analgesia in a mammal.
CC These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC tissue. This is shown by the peptides ability to stimulate contraction in
CC guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC neuronal tissue. OCTs are components of peptide toxins derived from
CC marine snails of the genus Conus, and act as calcium channel blockers.
CC These OCTs may be used to replace opiods in the treatment of chronic pain
CC or to reduce the opiod dosage required. This helps to reduce dependence
CC on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC PN field.)
XX
SQ Sequence 27 AA;

Query Match 78.0%; Score 117; DB 2; Length 27;
Best Local Similarity 73.1%; Pred. No. 7.2e-07;
Matches 19; Conservative 3; Mismatches 4; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| | ||||| |||||||||| |:::|
Db 1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26

RESULT 28
AAR37759
ID AAR37759 standard; peptide; 27 AA.
XX
AC AAR37759;
XX
DT 25-MAR-2003 (revised)
DT 08-SEP-1993 (first entry)
XX
DE TVIA/SNX-185.
XX
KW Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW N-channel mediated neurotransmitter release.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Modified-site 4
FT /note= "hydroxyproline"
FT Disulfide-bond 8. .19
FT Modified-site 10
FT /note= "hydroxyproline"
FT Disulfide-bond 15. .26
FT Modified-site 21
FT /note= "hydroxyproline"
XX
PN WO9310145-A1.
XX
PD 27-MAY-1993.
XX
PF 12-NOV-1992; 92WO-US009766.
XX
PR 12-NOV-1991; 91US-00789913.
PR 17-JUL-1992; 92US-00916478.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bowersox SS, Fox JA, Valentino KL, Bitner RS;
PI Yamashiro DH;
XX
DR WPI; 1993-182487/22.
XX
PT Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS Disclosure; Fig 1; 103pp; English.
XX
CC Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC damage caused by stroke. By delaying admin. for some time (compare
CC US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC in blood pressure caused by (I)). (I) is also at least as effective as
CC the specified conotoxins for (1) selective inhibition of N-type voltage-
CC gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC channel mediated neurotransmitter release in neuronal tissue. Primary
CC sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC correct PN field.)
XX
SQ Sequence 27 AA;

Query Match 78.0%; Score 117; DB 2; Length 27;
Best Local Similarity 73.1%; Pred. No. 7.2e-07;
Matches 19; Conservative 3; Mismatches 4; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| | ||||| |||||||||| |:::|
Db 1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26

RESULT 29
AAR76095
ID AAR76095 standard; peptide; 27 AA.
XX
AC AAR76095;
XX
DT 27-AUG-2003 (revised)
DT 25-MAR-2003 (revised)
DT 02-FEB-1996 (first entry)
XX
DE Omega conotoxin TVIA peptide.
XX
KW Omega conotoxin; marine snail; Conus; voltage-gated Ca channel blocker;
KW synaptosome; membrane; fish electric organ; mammalian brain; ischaemia;
KW binding protein; binding affinity; stroke.
XX
OS Conus.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Modified-site 4
FT /label= 4-Hyp
FT Disulfide-bond 8. .19
FT Modified-site 10

```
FT                   /label= 4-Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4-Hyp
FT   Modified-site   27
FT                   /note= "amidated C-terminus"
XX
PN   US5424218-A.
XX
PD   13-JUN-1995.
XX
PF   04-NOV-1993;   93US-00147714.
XX
PR   22-NOV-1989;   89US-00440094.
PR   02-AUG-1990;   90US-00561766.
PR   23-MAR-1992;   92US-00855269.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Valentino KL,  Bowersox SS,  Bitner RS,  Miljanich GP,  Yamashiro DH;
PI   Fox JA;
XX
DR   WPI; 1995-223694/29.
XX
PT   Identifying cpds. able to reduce neuronal damage caused by ischaemia - by
PT   measuring their affinity to omega conotoxin MVIIA binding site and
PT   ability e.g. to inhibit voltage gated calcium channels.
XX
PS   Disclosure; Fig 1; 31pp; English.
XX
CC   The peptides AAR76089-95 are naturally occuring omega conotoxin (OCT)
CC   peptides derived from marine snails of the Conus genus. The peptide
CC   sequences were used to chemically synthesise the OCT peptide fragments
CC   AAR76096-R76109. The OCT peptides act as voltage-gated Ca channel
CC   blockers by binding to a 210 kD protein from synaptosomal membrane
CC   preparations from fish electric organ or mammalian brains. The peptides
CC   and their synthesised fragments can be used to screen for compounds that
CC   bind to the OCT binding protein, by displacing a high affinity labelled
CC   OCT, such as MVIIA, from a synaptosomal membrane preparation. The
CC   compounds should have binding affinities and activities at least equal to
CC   those of the natural peptides (Ki 0.44-324 nM). The screened compounds
CC   are potentially useful in treating ischaemic conditions, esp. stroke, and
CC   can reduce sec. anatomical and functional damage associated with those
CC   conditions. (Updated on 25-MAR-2003 to correct PF field.) (Updated on 27-
CC   AUG-2003 to correct OS field.)
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 30
AAW19550
ID   AAW19550 standard; peptide; 27 AA.
XX
AC   AAW19550;
XX
DT   27-AUG-2003  (revised)
DT   13-OCT-1997  (first entry)
XX
DE   Natural omega-conopeptide TVIA/SNX-185 used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Conus.
XX
```

```
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /label= 4Hyp
FT   Misc-difference 10
FT                   /label= 4Hyp
FT   Misc-difference 21
FT                   /label= 4Hyp
FT   Modified-site   27
FT                   /note= "optionally amidated"
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Claim 3; Fig 2; 47pp; English.
XX
CC   AAW19544-W19553 are naturally occurring omega conopeptides (OCs) isolated
CC   from Conus sp. (cone snails). The peptides and their analogues are used
CC   as analgesics acting by blocking N-type voltage-sensitive calcium
CC   channels. The OCs can be used to treat neuropathic pain as a result of
CC   e.g. insult to the spinal cord or peripheral nerves, cancer, bone
CC   degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes zoster
CC   neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage. (Updated on 27-AUG-2003 to
CC   correct OS field.)
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 31
AAW72611
ID   AAW72611 standard; peptide; 27 AA.
XX
AC   AAW72611;
XX
DT   27-AUG-2003  (revised)
DT   06-JAN-1999  (first entry)
XX
DE   Conus genus natural omega-conopeptide TVIA/SNX-185.
XX
KW   Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW   nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW   inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
```

```
KW   rheumatoid arthritis; epilepsy.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   10
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   21
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
XX
PN   US5824645-A.
XX
PD   20-OCT-1998.
XX
PF   01-NOV-1996;   96US-00742774.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Valentino KL,  Gohil KC,  Justice A,  Singh T;
XX
DR   WPI; 1998-582596/49.
XX
PT   Treatment of inflammation, comprises administration of omega-conopeptide
PT   - effective to block voltage-gated calcium channels, bind with high
PT   affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT   release.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   A method has been developed for the treatment of inflammation in a
CC   subject. The method comprises administration of an omega-conopeptide
CC   effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC   high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC   neurotransmitter release from nervous tissue. The method is used to treat
CC   inflammation and associated pain. The treatment can also be used to
CC   produce analgesia (especially in subjects experiencing neuropathic pain);
CC   and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC   reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC   represents a natural omega-conopeptide. Omega-conopeptides are components
CC   of peptide toxins produced by marine snails of the genus Conus, and which
CC   act as calcium channel blockers. (Updated on 27-AUG-2003 to correct OS
CC   field.)
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 32
AAW95570
ID   AAW95570 standard; protein; 27 AA.
XX
AC   AAW95570;
XX
DT   29-MAR-1999  (first entry)
XX
DE   Omega-conopeptide TVIA/SNX-185.
XX
KW   Omega-conopeptide; peptide toxin; snail; calcium channel blocker;
KW   analgesia; guinea pig ileum; omega-conotoxin; pain; neuropathic.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   10
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   21
FT                   /label= 4Hyp
FT                   /note= "4-Hydroxyproline"
FT   Modified-site   27
FT                   /note= "C-terminal amide"
XX
PN   US5859186-A.
XX
PD   12-JAN-1999.
XX
PF   03-JUL-1996;   96US-00675354.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Gohil KC,  Valentino KL,  Justice A,  Singh T;
XX
DR   WPI; 1999-120002/10.
XX
PT   Production of analgesia in mammal - by administration of omega cono-
PT   peptide(s).
XX
PS   Disclosure; Fig 1B; 59pp; English.
XX
CC   Sequences AAW95564-573 represent primary sequences of natural omega-
CC   conopeptides. Omega-conopeptides are components of peptide toxins
CC   produced by marine snails of the genus Conus, and which act as calcium
CC   channel blockers. The invention relates to a method of producing
CC   analgesia in a mammal that comprises administering an omega conopeptide
CC   having activities in (a) inhibiting electrically stimulated contraction
CC   of guinea pig ileum and (b) selectively binding to omega conopeptide
CC   MVIIA binding sites in neuronal tissue, where these activities are within
CC   the ranges of those of omega-conotoxins MVIIA and TVIA. The method is
CC   used for treating chronic pain, especially neuropathic pain
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 33
AAY42340
ID   AAY42340 standard; peptide; 27 AA.
XX
AC   AAY42340;
XX
DT   20-DEC-1999  (first entry)
XX
DE   Omega-conotoxin OCT TVIA.
XX
KW   Calcium channel; neuron; retina; optic nerve; trauma; ischaemia; vision;
KW   prevention.
```

```
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4Hyp
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= 4Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4Hyp
FT   Misc-difference 25
FT                   /note= "Optionally contains C-terminal amide"
XX
PN   US5965534-A.
XX
PD   12-OCT-1999.
XX
PF   13-MAR-1998;   98US-00039168.
XX
PR   22-NOV-1995;   95US-00562142.
XX
PA   (ALCO-) ALCON LAB INC.
XX
PI   Hellberg M,  Pang I,  Kapin M;
XX
DR   WPI; 1999-579926/49.
XX
PT   Treatment or prevention of retinal or optic nerve head damage comprises
PT   administration of an omega-conotoxin derivative.
XX
PS   Claim 2; Col 11-12; 7pp; English.
XX
CC   This sequence represents omega-conotoxin OCT TVIA. Omega-conotoxins
CC   selectively block N-type calcium channels responsible for calcium influx
CC   in neurons. Acute retinal or optic nerve damage, which can result in the
CC   loss of vision, is caused by acute trauma and pathological events such as
CC   ischaemia, hypoxia or oedema. The release of excitatory amino acids is
CC   implicated in ischaemia-related neuronal and retinal damage, with
CC   excitatory amino acid release leading to excessive stimulation of post-
CC   synaptic excitatory amino acid receptors, which can result in cell
CC   injury. The release of such excitatory amino acids from presynaptic nerve
CC   terminals is dependent upon an elevation of calcium in the nerve
CC   terminal. This presynaptic calcium influx is mediated by the N-type
CC   calcium channels that are inhibited by omega-conotoxins. Intraocular
CC   administration of at least one omega-conotoxin could be used for the
CC   treatment or prevention of retinal or optic nerve head damage resulting
CC   from acute traumatic or acute ischaemic events
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 34
AAB14358
ID   AAB14358 standard; peptide; 27 AA.
XX
AC   AAB14358;
XX
DT   06-DEC-2000  (first entry)
XX
DE   Omega-conopeptide TVIA/SNX-185.
XX
KW   Marine snail; omega-conopeptide; calcium channel blocker; TVIA; SNX-185;
KW   toxin; analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW   norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW   acute dystonic reaction; inflammation; epilepsy.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4Hyp
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= 4Hyp
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4Hyp
FT   Modified-site   27
FT                   /note= "C-terminal amide"
XX
PN   US6087091-A.
XX
PD   11-JUL-2000.
XX
PF   23-APR-1999;   99US-00298017.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2000-490177/43.
XX
PT   Selecting a compound for producing analgesia involves measuring activity
PT   of test compound in blocking voltage-gated calcium channels, binding to
PT   omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   The present sequence is an omega-conopeptide from marine snails of the
CC   genus Conus. Omega-conopeptides are components of peptide toxins produced
CC   by the cone snails, and which act as calcium channel blockers. Natural
CC   omega-conopeptides and their derivatives may be useful for producing
CC   analgesia in nociceptive and neuropathic pain. The peptides bind to omega
CC   -conopeptide binding sites, which are present mainly in neuronal tissue,
CC   and inhibit norepinephrine release from nervous tissue. Conopeptides such
CC   as MVIIA and TVIA are effective as therapeutic agents for treating
CC   neurogenic conditions such as schizophrenia, tardive dyskinesia and acute
CC   dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 3;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 35
AAB19448
ID   AAB19448 standard; peptide; 27 AA.
XX
AC   AAB19448;
XX
DT   06-MAR-2001  (first entry)
XX
```

```
DE   Primary sequence of a natural omega-conopeptide TVIA/SNX-185.
XX
KW   Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW   peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW   schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW   epilepsy.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  8. .19
FT   Modified-site   10
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= Hyp
FT                   /note= "hydroxyproline"
FT   Modified-site   27
FT                   /note= "amidated C-terminal"
XX
PN   US6136786-A.
XX
PD   24-OCT-2000.
XX
PF   09-SEP-1999;   99US-00392979.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   23-JUN-1993;   93US-00081863.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
PR   23-APR-1999;   99US-00298017.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2001-030946/04.
XX
PT   Enhancing analgesia produced by opiates by administering an omega-
PT   conopeptide that inhibits electrically stimulated contraction of guinea
PT   pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT   tissues.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   The present sequence represents an omega-conopeptide. Omega-conopeptides
CC   are components of peptide toxins which act as voltage-gated calcium
CC   channel inhibitors. The peptides are used to enhance the analgesic effect
CC   produced by an opiate in a mammalian subject. The method comprises
CC   administering to the subject an omega-conopeptide which is able to
CC   inhibit electrically stimulated contraction of the guinea pig ileum and
CC   bind to omega-conopeptide MVIIA binding sites present in neuronal tissue.
CC   Omega-conopeptides are useful for enhancing the analgesic effect produced
CC   by an opiate. Omega-conopeptides may also be used in the treatment of
CC   pain, in reducing neuronal damage related to an ischemic condition in
CC   mammals, and in treating schizophrenia, tardive dyskinesia and acute
CC   dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 27 AA;

  Query Match             78.0%;  Score 117;  DB 4;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 7.2e-07;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| ||:::|
Db          1 CLSPGSSCSPTSYNCCRSCNPYSRKC 26


RESULT 36
ABB96688
ID   ABB96688 standard; peptide; 73 AA.
XX
AC   ABB96688;
XX
DT   12-JUL-2002  (first entry)
XX
DE   Omega-conopeptide w-TVIA propeptide.
XX
KW   Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW   neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW   antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW   anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW   neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW   stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW   drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW   migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW   psychosis; anxiety; schizophrenia.
XX
OS   Conus tulipa.
XX
PN   WO200207675-A2.
XX
PD   31-JAN-2002.
XX
PF   23-JUL-2001; 2001WO-US023041.
XX
PR   21-JUL-2000; 2000US-0219616P.
PR   05-FEB-2001; 2001US-0265888P.
XX
PA   (UTAH ) UNIV UTAH RES FOUND.
PA   (COGN-) COGNETIX INC.
XX
PI   Olivera BM,  Mcintosh JM,  Watkins M,  Garrett JE,  Shon K;
PI   Jacobsen R,  Jones RM,  Cartier GE;
XX
DR   WPI; 2002-257318/30.
DR   N-PSDB; ABL98947.
XX
PT   New omega-conopeptides useful for treating disorders associated with
PT   voltage gated ion channels e.g. pain, inflammation, neurologic or
PT   cardiovascular disorders.
XX
PS   Claim 1(c); Page 66; 195pp; English.
XX
CC   The invention relates to isolated omega-conopeptides, nucleic acid
CC   sequences encoding them, and propeptide sequences. The activity of the
CC   peptides of the invention may be described as, analgesic, anticonvulsant,
CC   vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC   antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC   antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC   by modulating the activity of voltage gated ion channels. They may be
CC   used for treating or preventing disorders associated with voltage gated
CC   ion channels such as neurological disorders, e.g. seizure (associated
CC   with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC   anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC   chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC   events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC   They may also be used for treating psychiatric disorders e.g. psychosis,
CC   anxiety or schizophrenia. The analgesic agents of the invention show
CC   diminished side effects and toxicity, and are non-addictive. The
CC   sequences given in records ABB96595-ABB96697 represent omega-conopeptide
CC   propeptide sequences
XX
SQ   Sequence 73 AA;

  Query Match             78.0%;  Score 117;  DB 5;  Length 73;
  Best Local Similarity   73.1%;  Pred. No. 1.7e-06;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;
```

```
Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |:::|
Db         46 CLSPGSSCSPTSYNCCRSCNPYSRKC 71
```

RESULT 37
ABB96743
ID ABB96743 standard; peptide; 27 AA.
XX
AC ABB96743;
XX
DT 12-JUL-2002 (first entry)
XX
DE Omega-conopeptide G6.1 generic toxin sequence.
XX
KW Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW psychosis; anxiety; schizophrenia.
XX
OS Conus geographus.
XX
FH Key   Location/Qualifiers
FT Misc-difference 4
FT   /label= OTHER
FT   /note= "OTHER is Pro or Hydroxy Pro"
FT Misc-difference 10
FT   /label= OTHER
FT   /note= "OTHER is Pro or Hydroxy Pro"
FT Misc-difference 13
FT   /label= OTHER
FT   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT Misc-difference 21
FT   /label= OTHER
FT   /note= "OTHER is Pro or Hydroxy Pro"
FT Misc-difference 22
FT   /label= OTHER
FT   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
FT Misc-difference 27
FT   /label= OTHER
FT   /note= "OTHER is Tyr, 125I-Tyr, mono-iodo-Tyr or di-iodo-
FT   Tyr or O-sulpho-Tyr or O-Phospho-Tyr"
XX
PN WO200207675-A2.
XX
PD 31-JAN-2002.
XX
PF 23-JUL-2001; 2001WO-US023041.
XX
PR 21-JUL-2000; 2000US-0219616P.
PR 05-FEB-2001; 2001US-0265888P.
XX
PA (UTAH) UNIV UTAH RES FOUND.
PA (COGN-) COGNETIX INC.
XX
PI Olivera BM, Mcintosh JM, Watkins M, Garrett JE, Shon K;
PI Jacobsen R, Jones RM, Cartier GE;
XX
DR WPI; 2002-257318/30.
XX
PT New omega-conopeptides useful for treating disorders associated with
PT voltage gated ion channels e.g. pain, inflammation, neurologic or
PT cardiovascular disorders.
XX
PS Example 2; Page 43; 195pp; English.
XX
CC The invention relates to isolated omega-conopeptides, nucleic acid
CC sequences encoding them, and propeptide sequences. The activity of the
CC peptides of the invention may be described as, analgesic, anticonvulsant,
CC vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC by modulating the activity of voltage gated ion channels. They may be
CC used for treating or preventing disorders associated with voltage gated
CC ion channels such as neurological disorders, e.g. seizure (associated
CC with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC They may also be used for treating psychiatric disorders e.g. psychosis,
CC anxiety or schizophrenia. The analgesic agents of the invention show
CC diminished side effects and toxicity, and are non-addictive. The
CC sequences given in records ABB96698-ABB96806 represent omega-conopeptide
CC generic toxin sequences
XX
SQ Sequence 27 AA;

```
  Query Match             77.3%;  Score 116;  DB 5;  Length 27;
  Best Local Similarity   88.5%;  Pred. No. 9.5e-07;
  Matches   23;  Conservative    0;  Mismatches    3;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              |||||||||||| ||||||||  |||
Db          1 CKSXGSSCSXTSXNCCRSCNXXAKRC 26
```

RESULT 38
AAB92218
ID AAB92218 standard; peptide; 24 AA.
XX
AC AAB92218;
XX
DT 22-JUN-2001 (first entry)
XX
DE Toxin peptide SEQ ID NO:1394.
XX
KW Protection; endogenous therapeutic peptide; peptidase; conjugation;
KW blood component; modification; succinimidyl; maleimido group; amino;
KW hydroxyl; thiol; hormone; growth factor; neurotransmitter.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO200069900-A2.
XX
PD 23-NOV-2000.
XX
PF 17-MAY-2000; 2000WO-US013576.
XX
PR 17-MAY-1999; 99US-0134406P.
PR 10-SEP-1999; 99US-0153406P.
PR 15-OCT-1999; 99US-0159783P.
XX
PA (CONJ-) CONJUCHEM INC.
XX
PI Bridon DP, Ezrin AM, Milner PG, Holmes DL, Thibaudeau K;
XX
DR WPI; 2001-112059/12.
XX
PT Modifying and attaching therapeutic peptides to albumin prevents
PT peptidase degradation, useful for increasing length of in vivo activity.
XX
PS Disclosure; Page 652; 733pp; English.
XX
CC The present invention describes a modified therapeutic peptide (I)
CC comprising a therapeutically active amino acid region (III) and a
CC reactive group (II) (e.g. succinimidyl and maleimido groups) attached to
CC a less therapeutically active amino acid region (IV), which covalently

CC bonds with amino/hydroxyl/thiol groups on blood components to form a
CC peptidase stabilised therapeutic peptide composed of 3-50 amino acids.
CC (I) are useful for modifying therapeutic peptides e.g. hormones, growth
CC factors and neurotransmitters, to protect them from peptidase activity in
CC vivo for the treatment of various disorders. Endogenous therapeutic
CC peptides are not suitable as drug candidates as they require frequent
CC administration due to rapid degradation by peptidases in the body.
CC Modifying and attaching therapeutic peptides to albumin prevents or
CC reduces the action of peptidases to increase length of activity (half
CC life) and specificity as bonding to large molecules decreases
CC intracellular uptake and interference with physiological processes.
CC AAB90829 to AAB92441 represent peptides which can be used in the
CC exemplification of the present invention
XX
SQ Sequence 24 AA;

Query Match 77.0%; Score 115.5; DB 4; Length 24;
Best Local Similarity 88.9%; Pred. No. 9.8e-07;
Matches 24; Conservative 0; Mismatches 0; Indels 3; Gaps 3;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRCY 27
||| ||||| |||||||||| ||||||
Db 1 CKS-GSSCS-TSYNCCRSCN-YTKRCY 24

RESULT 39
AAR38517
ID AAR38517 standard; peptide; 27 AA.
XX
AC AAR38517;
XX
DT 12-NOV-1993 (first entry)
XX
DE Omega-conotoxin neurotoxin peptide (2).
XX
KW Omega-conotoxin; neurotoxin; peptide; Conus; lung disease; bronchitis;
KW N-channel; calcium; allergy; airway hyperreactivity; farmers lung;
KW extrinsic asthma; industrial asthma; antagonist; pigeon fanciers lung;
KW chronic obstructive pulmonary disease; venom; viral infection.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Misc-difference 2
FT /label= LYS, LEU
FT Misc-difference 4
FT /note= "Unspecified amino acid"
FT Misc-difference 10
FT /note= "Unspecified amino acid"
FT Misc-difference 21
FT /note= "Unspecified amino acid"
FT Misc-difference 23
FT /label= SER, THR
FT Misc-difference 24
FT /label= LYS, ARG
FT Misc-difference 25
FT /label= LYS, ARG
FT Misc-difference 27
FT /label= TYR, ARG
FT /note= "May opt. be amidated"
XX
PN GB2262886-A.
XX
PD 07-JUL-1993.
XX
PF 17-DEC-1991; 91GB-00026739.
XX
PR 17-DEC-1991; 91GB-00026739.
XX
PA (ELIL) LILLY IND LTD.
XX
PI Bond A, Boot JR;
XX
DR WPI; 1993-215931/27.
XX
PT N-channel calcium antagonists, e.g. conotoxin peptide(s) - used for
PT treating diseases which cause bronchoconstriction.
XX
PS Disclosure; Page 2; 9pp; English.
XX
CC The sequences given in R3856-17 are omega-conotoxin neurotoxin peptides
CC which have been isolated from Conus venom. These peptides act as N-
CC channel calcium antagonists and may be used for treating allergic lung
CC diseases such as extrinsic asthma and industrial asthmas eg. farmers lung
CC and pigeon fanciers lung. They may also be used to treat other
CC inflammatory disorders such as chronic obstructive pulmonary disease and
CC bronchitis, or airway hyperreactivity caused by viral infection
XX
SQ Sequence 27 AA;

Query Match 76.0%; Score 114; DB 2; Length 27;
Best Local Similarity 84.6%; Pred. No. 1.6e-06;
Matches 22; Conservative 0; Mismatches 4; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| |||||||||||||||||||| |
Db 1 CXSXGSSCSXTSYNCCRSCNXYXXXC 26

RESULT 40
ABB96856
ID ABB96856 standard; peptide; 30 AA.
XX
AC ABB96856;
XX
DT 07-AUG-2003 (revised)
DT 12-JUL-2002 (first entry)
XX
DE Omega-conopeptide L6.1 toxin sequence.
XX
KW Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW psychosis; anxiety; schizophrenia.
XX
OS Conus sp.
XX
PN WO200207675-A2.
XX
PD 31-JAN-2002.
XX
PF 23-JUL-2001; 2001WO-US023041.
XX
PR 21-JUL-2000; 2000US-0219616P.
PR 05-FEB-2001; 2001US-0265888P.
XX
PA (UTAH) UNIV UTAH RES FOUND.
PA (COGN-) COGNETIX INC.
XX
PI Olivera BM, Mcintosh JM, Watkins M, Garrett JE, Shon K;
PI Jacobsen R, Jones RM, Cartier GE;
XX
DR WPI; 2002-257318/30.
XX
PT New omega-conopeptides useful for treating disorders associated with
PT voltage gated ion channels e.g. pain, inflammation, neurologic or
PT cardiovascular disorders.
XX
PS Claim 1(a); Page 72; 195pp; English.
XX
CC The invention relates to isolated omega-conopeptides, nucleic acid

CC sequences encoding them, and propeptide sequences. The activity of the
CC peptides of the invention may be described as, analgesic, anticonvulsant,
CC vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC by modulating the activity of voltage gated ion channels. They may be
CC used for treating or preventing disorders associated with voltage gated
CC ion channels such as neurological disorders, e.g. seizure (associated
CC with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC They may also be used for treating psychiatric disorders e.g. psychosis,
CC anxiety or schizophrenia. The analgesic agents of the invention show
CC diminished side effects and toxicity, and are non-addictive. The
CC sequences given in records ABB96807-ABB96905 represent omega-conopeptide
CC toxin sequences. (Updated on 07-AUG-2003 to correct OS field.)
XX
SQ Sequence 30 AA;

Query Match 74.7%; Score 112; DB 5; Length 30;
Best Local Similarity 69.2%; Pred. No. 3e-06;
Matches 18; Conservative 2; Mismatches 6; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
||| || || |||||| |: |||:|
Db 1 CKSPGSPCSVTSYNCCTFCSSYTKKC 26

RESULT 41
ABB96653
ID ABB96653 standard; peptide; 75 AA.
XX
AC ABB96653;
XX
DT 12-JUL-2002 (first entry)
XX
DE Omega-conopeptide L6.1 propeptide.
XX
KW Omega-conopeptide; analgesic; anticonvulsant; vasotropic; cardiant;
KW neuroprotective; cerebroprotective; cardiovascular; antiinflammatory;
KW antimigraine; antidiabetic; tranquiliser; vulnerary; antipsychotic;
KW anxiolytic; neuroleptic; voltage gated ion channel; seizure; epilepsy;
KW neurological disorder; neurotoxic injury; hypoxia; anoxia; ischaemia;
KW stroke; cerebrovascular accident; brain trauma; spinal chord trauma;
KW drowning; suffocation; perinatal asphyxia; hypoglycaemic event; pain;
KW migraine; inflammation; cardiovascular disorder; psychiatric disorder;
KW psychosis; anxiety; schizophrenia.
XX
OS Conus leopardus.
XX
PN WO200207675-A2.
XX
PD 31-JAN-2002.
XX
PF 23-JUL-2001; 2001WO-US023041.
XX
PR 21-JUL-2000; 2000US-0219616P.
PR 05-FEB-2001; 2001US-0265888P.
XX
PA (UTAH) UNIV UTAH RES FOUND.
PA (COGN-) COGNETIX INC.
XX
PI Olivera BM, Mcintosh JM, Watkins M, Garrett JE, Shon K;
PI Jacobsen R, Jones RM, Cartier GE;
XX
DR WPI; 2002-257318/30.
DR N-PSDB; ABL98912.
XX
PT New omega-conopeptides useful for treating disorders associated with
PT voltage gated ion channels e.g. pain, inflammation, neurologic or
PT cardiovascular disorders.
XX
PS Claim 1(c); Page 50; 195pp; English.
XX
CC The invention relates to isolated omega-conopeptides, nucleic acid
CC sequences encoding them, and propeptide sequences. The activity of the
CC peptides of the invention may be described as, analgesic, anticonvulsant,
CC vasotropic, cardiant, neuroprotective, cerebroprotective, cardiovascular,
CC antiinflammatory, antimigraine, antidiabetic, tranquiliser, vulnerary,
CC antipsychotic, anxiolytic and neuroleptic. Peptides of the invention act
CC by modulating the activity of voltage gated ion channels. They may be
CC used for treating or preventing disorders associated with voltage gated
CC ion channels such as neurological disorders, e.g. seizure (associated
CC with epilepsy), neurotoxic injury associated with conditions of hypoxia,
CC anoxia, ischaemia, stroke, cerebrovascular accident, brain or spinal
CC chord trauma, drowning, suffocation, perinatal asphyxia or hypoglycaemic
CC events; pain e.g. migraine; inflammation or cardiovascular disorders.
CC They may also be used for treating psychiatric disorders e.g. psychosis,
CC anxiety or schizophrenia. The analgesic agents of the invention show
CC diminished side effects and toxicity, and are non-addictive. The
CC sequences given in records ABB96595-ABB96697 represent omega-conopeptide
CC propeptide sequences
XX
SQ Sequence 75 AA;

Query Match 74.7%; Score 112; DB 5; Length 75;
Best Local Similarity 69.2%; Pred. No. 6.6e-06;
Matches 18; Conservative 2; Mismatches 6; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
||| || || |||||| |: |||:|
Db 46 CKSPGSPCSVTSYNCCTFCSSYTKKC 71

RESULT 42
AAR12543
ID AAR12543 standard; protein; 27 AA.
XX
AC AAR12543;
XX
DT 23-SEP-2004 (revised)
DT 05-SEP-1991 (first entry)
XX
DE Omega conotoxin peptide #2.
XX
KW neuronal calcium-channel antagonist; OCT; adrenaline release.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Misc-difference 2
FT /label= Lys, Leu
FT /note= "see comments for provisos"
FT Misc-difference 4
FT /label= 4Hyp
FT Disulfide-bond 8. .19
FT Misc-difference 10
FT /label= 4Hyp
FT Disulfide-bond 15. .26
FT Misc-difference 21
FT /label= 4Hyp
FT Misc-difference 23
FT /label= Thr, Ser
FT /note= "see comments for provisos"
FT Misc-difference 24
FT /label= Lys, Arg
FT /note= "see comments for provisos"
FT Misc-difference 25
FT /label= Arg, Lys
FT /note= "see comments for provisos"
FT Misc-difference 27
FT /label= Tyr, Arg
FT /note= "see comments for provisos"
XX

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PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Claim 13; Page 59; 74pp; English.
XX
CC   This generic OCT peptide excludes the peptides having the following
CC   combinations of amino acids at the variable positions: K(2), T(23),
CC   K(24), R(25) and Y(27); and L(2), S(23), R(24), K(25) and R(27). Specific
CC   peptides which are covered by this generic formula can bind to neuronal
CC   membrane OCT MVIIA binding sites with a binding activity in the range of
CC   such activity for MVIIA, GVIA and TVIA. They are used in a pharmaceutical
CC   composition with a sterile injectable medium to reduce neuronal damage
CC   related to an ischaemic condition in a mammal. The disulphide bonds,
CC   although not directly indicated on the published formula, are described
CC   in the disclosure. See also AAR12542, AAR12544-7 and AAR13264-6
CC
CC   Revised record issued on 23-SEP-2004 : Correction to Feature Table Key
XX
SQ   Sequence 27 AA;

  Query Match             74.0%;  Score 111;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 3.6e-06;
  Matches   19;  Conservative    0;  Mismatches    7;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | | ||||| |||||||||| |   |
Db          1 CXSPGSSCSPTSYNCCRSCNPYXXXC 26


RESULT 43
AAW12986
ID   AAW12986 standard; peptide; 27 AA.
XX
AC   AAW12986;
XX
DT   25-MAR-2003  (revised)
DT   22-APR-1997  (first entry)
XX
DE   Omega conopeptide SNX-207.
XX
KW   Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW   neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW   acute dystonic reactions; inflammation; epilepsy.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Hyp
FT   Modified-site   21
FT                   /label= Hyp
XX
PN   US5587454-A.
XX
PD   24-DEC-1996.
XX
PF   15-APR-1993;   93US-00049794.
XX
PR   30-DEC-1991;   91US-00814759.
PR   30-DEC-1992;   92WO-US011349.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Gohil KC,  Miljanich GP,  Valentino KL,  Justice A,  Singh T;
XX
DR   WPI; 1997-064830/06.
XX
PT   Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT   neuropathic pain.
XX
PS   Disclosure; Col 53-54; 58pp; English.
XX
CC   The present peptide is an omega conopeptide, useful as an analgesic,
CC   especially for treating neuropathic pain. The peptide, which can be
CC   prepared by solid phase synthesis, can also be used to inhibit neuronal
CC   damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC   reactions, inflammation and epilepsy. (Updated on 25-MAR-2003 to correct
CC   PF field.)
XX
SQ   Sequence 27 AA;

  Query Match             72.7%;  Score 109;  DB 2;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 6.2e-06;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | |||||||   ||||||||||:::|
Db          1 CLSXGSSCSRLMYNCCRSCNXYSRKC 26


RESULT 44
AAY56497
ID   AAY56497 standard; peptide; 27 AA.
XX
AC   AAY56497;
XX
DT   16-FEB-2000  (first entry)
XX
DE   Analogue omega conopeptide SNX-207.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Misc-difference 4
FT                   /note= "unspecified"
FT   Disulfide-bond  8. .19
FT   Misc-difference 10
FT                   /note= "unspecified"
FT   Disulfide-bond  15. .26
FT   Misc-difference 21
FT                   /note= "unspecified"
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
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XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
PT   inflammation.
XX
PS   Disclosure; Fig 2; 47pp; English.
XX
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 27 AA;

  Query Match             72.7%;  Score 109;  DB 3;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 6.2e-06;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | |||||||   ||||||||||:::|
Db          1 CLSXGSSCSRLMYNCCRSCNXYSRKC 26


RESULT 45
AAB14371
ID   AAB14371 standard; peptide; 27 AA.
XX
AC   AAB14371;
XX
DT   06-DEC-2000  (first entry)
XX
DE   Omega-conopeptide SNX-207.
XX
KW   Marine snail; omega-conopeptide; calcium channel blocker; SNX-207; toxin;
KW   analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW   norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW   acute dystonic reaction; inflammation; epilepsy.
XX
OS   Conus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Modified-site   4
FT                   /label= 4Hyp
FT   Disulfide-bond  8. .19
FT   Disulfide-bond  15. .26
FT   Modified-site   21
FT                   /label= 4Hyp
FT   Modified-site   27
FT                   /note= "C-terminal amide"
XX
PN   US6087091-A.
XX
PD   11-JUL-2000.
XX
PF   23-APR-1999;   99US-00298017.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2000-490177/43.
XX
PT   Selecting a compound for producing analgesia involves measuring activity
PT   of test compound in blocking voltage-gated calcium channels, binding to
PT   omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS   Disclosure; Fig 2; 58pp; English.
XX
CC   The present sequence is an omega-conopeptide analogue. Omega-conopeptides
CC   are components of peptide toxins produced marine snails of the genus
CC   Conus. Omega-conopeptides and their derivatives act as calcium channel
CC   blockers and may be useful for producing analgesia in nociceptive and
CC   neuropathic pain. The peptides bind to omega-conopeptide binding sites,
CC   which are present mainly in neuronal tissue, and inhibit norepinephrine
CC   release from nervous tissue. Conopeptides such as MVIIA and TVIA are
CC   effective as therapeutic agents for treating neurogenic conditions such
CC   as schizophrenia, tardive dyskinesia and acute dystonic reactions,
CC   inflammation and epilepsy
XX
SQ   Sequence 27 AA;

  Query Match             72.7%;  Score 109;  DB 3;  Length 27;
  Best Local Similarity   73.1%;  Pred. No. 6.2e-06;
  Matches   19;  Conservative    3;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | |||||||   ||||||||||:::|
Db          1 CLSXGSSCSRLMYNCCRSCNXYSRKC 26


RESULT 46
AAW12996
ID   AAW12996 standard; peptide; 27 AA.
XX
AC   AAW12996;
XX
DT   25-MAR-2003  (revised)
DT   22-APR-1997  (first entry)
XX
DE   Omega conopeptide SNX-236.
XX
KW   Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW   neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW   acute dystonic reactions; inflammation; epilepsy.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /note= "undefined"
XX
PN   US5587454-A.
XX
PD   24-DEC-1996.
XX
PF   15-APR-1993;   93US-00049794.
XX
PR   30-DEC-1991;   91US-00814759.
PR   30-DEC-1992;   92WO-US011349.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Gohil KC,  Miljanich GP,  Valentino KL,  Justice A,  Singh T;
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XX
DR   WPI; 1997-064830/06.
XX
PT   Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT   neuropathic pain.
XX
PS   Claim 1; Col 59-60; 58pp; English.
XX
CC   The present peptide is an omega conopeptide, useful as an analgesic,
CC   especially for treating neuropathic pain. The peptide, which can be
CC   prepared by solid phase synthesis, can also be used to inhibit neuronal
CC   damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC   reactions, inflammation and epilepsy. (Updated on 25-MAR-2003 to correct
CC   PF field.)
XX
SQ   Sequence 27 AA;

  Query Match             72.0%;  Score 108;  DB 2;  Length 27;
  Best Local Similarity   69.2%;  Pred. No. 8.2e-06;
  Matches   18;  Conservative    3;  Mismatches    5;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | |||||||   |||||||| |:::|
Db          1 CLSXGSSCSRLMYNCCRSCNPYSRKC 26


RESULT 47
AAW72627
ID   AAW72627 standard; peptide; 27 AA.
XX
AC   AAW72627;
XX
DT   27-AUG-2003  (revised)
DT   06-JAN-1999  (first entry)
XX
DE   Conus genus analogue omega-conopeptide SNX-236.
XX
KW   Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW   nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW   inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
KW   rheumatoid arthritis; epilepsy.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 4
FT                   /note= "unspecified"
XX
PN   US5824645-A.
XX
PD   20-OCT-1998.
XX
PF   01-NOV-1996;   96US-00742774.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Valentino KL,  Gohil KC,  Justice A,  Singh T;
XX
DR   WPI; 1998-582596/49.
XX
PT   Treatment of inflammation, comprises administration of omega-conopeptide
PT   - effective to block voltage-gated calcium channels, bind with high
PT   affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT   release.
XX
PS   Disclosure; Fig 2; 58pp; English.
XX
CC   A method has been developed for the treatment of inflammation in a
CC   subject. The method comprises administration of an omega-conopeptide
CC   effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC   high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC   neurotransmitter release from nervous tissue. The method is used to treat
CC   inflammation and associated pain. The treatment can also be used to
CC   produce analgesia (especially in subjects experiencing neuropathic pain);
CC   and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC   reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC   represents an analogue omega-conopeptide. Omega-conopeptides are
CC   components of peptide toxins produced by marine snails of the genus
CC   Conus, and which act as calcium channel blockers. (Updated on 27-AUG-2003
CC   to correct OS field.)
XX
SQ   Sequence 27 AA;

  Query Match             72.0%;  Score 108;  DB 2;  Length 27;
  Best Local Similarity   69.2%;  Pred. No. 8.2e-06;
  Matches   18;  Conservative    3;  Mismatches    5;  Indels    0;  Gaps    0;

Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | |||||||   |||||||| |:::|
Db          1 CLSXGSSCSRLMYNCCRSCNPYSRKC 26


RESULT 48
AAY56498
ID   AAY56498 standard; peptide; 27 AA.
XX
AC   AAY56498;
XX
DT   16-FEB-2000  (first entry)
XX
DE   Analogue omega conopeptide SNX-236.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Misc-difference 4
FT                   /note= "unspecified"
FT   Disulfide-bond  8. .19
FT   Misc-difference 10
FT                   /note= "unspecified"
FT   Disulfide-bond  15. .26
FT   Misc-difference 21
FT                   /note= "unspecified"
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
```

PT inflammation.
XX
PS Disclosure; Fig 2; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 27 AA;

Query Match 72.0%; Score 108; DB 3; Length 27;
Best Local Similarity 69.2%; Pred. No. 8.2e-06;
Matches 18; Conservative 3; Mismatches 5; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| ||||||| ||||||| |:::|
Db 1 CLSXGSSCSRLMYNCCRSCNPYSRKC 26

RESULT 49
AAB14378
ID AAB14378 standard; peptide; 27 AA.
XX
AC AAB14378;
XX
DT 06-DEC-2000 (first entry)
XX
DE Omega-conopeptide SNX-236.
XX
KW Marine snail; omega-conopeptide; calcium channel blocker; SNX-236; toxin;
KW analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW acute dystonic reaction; inflammation; epilepsy.
XX
OS Conus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Modified-site 4
FT /label= 4Hyp
FT Disulfide-bond 8. .19
FT Disulfide-bond 15. .26
FT Modified-site 27
FT /note= "C-terminal amide"
XX
PN US6087091-A.
XX
PD 11-JUL-2000.
XX
PF 23-APR-1999; 99US-00298017.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2000-490177/43.
XX
PT Selecting a compound for producing analgesia involves measuring activity
PT of test compound in blocking voltage-gated calcium channels, binding to
PT omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS Disclosure; Fig 2; 58pp; English.
XX
CC The present sequence is an omega-conopeptide analogue. Omega-conopeptides
CC are components of peptide toxins produced marine snails of the genus
CC Conus. Omega-conopeptides and their derivatives act as calcium channel
CC blockers and may be useful for producing analgesia in nociceptive and
CC neuropathic pain. The peptides bind to omega-conopeptide binding sites,
CC which are present mainly in neuronal tissue, and inhibit norepinephrine
CC release from nervous tissue. Conopeptides such as MVIIA and TVIA are
CC effective as therapeutic agents for treating neurogenic conditions such
CC as schizophrenia, tardive dyskinesia and acute dystonic reactions,
CC inflammation and epilepsy
XX
SQ Sequence 27 AA;

Query Match 72.0%; Score 108; DB 3; Length 27;
Best Local Similarity 69.2%; Pred. No. 8.2e-06;
Matches 18; Conservative 3; Mismatches 5; Indels 0; Gaps 0;

Qy 1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
| ||||||| ||||||| |:::|
Db 1 CLSXGSSCSRLMYNCCRSCNPYSRKC 26

RESULT 50
AAB19464
ID AAB19464 standard; peptide; 27 AA.
XX
AC AAB19464;
XX
DT 06-MAR-2001 (first entry)
XX
DE Sequence of an omega-conopeptide analogue designated SNX-236.
XX
KW Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW epilepsy.
XX
OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Misc-difference 4
FT /note= "unspecified residue"
FT Modified-site 25
FT /note= "amidated residue"
XX
PN US6136786-A.
XX
PD 24-OCT-2000.
XX
PF 09-SEP-1999; 99US-00392979.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 23-JUN-1993; 93US-00081863.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
PR 23-APR-1999; 99US-00298017.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2001-030946/04.
XX
PT Enhancing analgesia produced by opiates by administering an omega-

PT conopeptide that inhibits electrically stimulated contraction of guinea
PT pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT tissues.
XX
PS Disclosure; Col 59-60; 58pp; English.
XX
CC The present sequence represents an omega-conopeptide analogue. Omega-
CC conopeptides are components of peptide toxins which act as voltage-gated
CC calcium channel inhibitors. The peptides are used to enhance the
CC analgesic effect produced by an opiate in a mammalian subject. The method
CC comprises administering to the subject an omega-conopeptide which is able
CC to inhibit electrically stimulated contraction of the guinea pig ileum
CC and bind to omega-conopeptide MVIIA binding sites present in neuronal
CC tissue. Omega-conopeptides are useful for enhancing the analgesic effect
CC produced by an opiate. Omega-conopeptides may also be used in the
CC treatment of pain, in reducing neuronal damage related to an ischemic
CC condition in mammals, and in treating schizophrenia, tardive dyskinesia
CC and acute dystonic reactions, inflammation and epilepsy
XX
SQ Sequence 27 AA;

Query Match 72.0%; Score 108; DB 4; Length 27;
Best Local Similarity 69.2%; Pred. No. 8.2e-06;
Matches 18; Conservative 3; Mismatches 5; Indels 0; Gaps 0;

```
Qy          1 CKSXGSSCSXTSYNCCRSCNXYTKRC 26
              | ||||||| |||||||| |:::|
Db          1 CLSXGSSCSRLMYNCCRSCNPYSRKC 26
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Search completed: March 28, 2005, 16:39:27
Job time : 73 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 28, 2005, 16:30:33 ; Search time 66.6667 Seconds
(without alignments)
145.035 Million cell updates/sec

Title: US-09-787-082A-11
Perfect score: 147
Sequence: 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 50 summaries

Database : A_Geneseq_16Dec04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	146	99.3	25	2	AAR39626	SNX-200.
2	146	99.3	25	2	AAR37771	Aar37771 SNX-200.
3	146	99.3	25	2	AAW19564	Aaw19564 SNX-200,
4	146	99.3	25	3	AAY56492	Aay56492 Analogue
5	145	98.6	25	2	AAR39608	Aar39608 MVIIA/SNX
6	145	98.6	25	2	AAR37752	Aar37752 MVIIA/SNX
7	145	98.6	25	2	AAR32777	Aar32777 MVIIA ome
8	145	98.6	25	2	AAR76089	Aar76089 Omega con
9	145	98.6	25	2	AAW19544	Aaw19544 Natural o
10	145	98.6	25	2	AAW19569	Aaw19569 SNX-279,
11	145	98.6	25	2	AAW12967	Aaw12967 Omega con
12	145	98.6	25	2	AAW72605	Aaw72605 Conus gen
13	145	98.6	25	2	AAW95564	Aaw95564 Omega-con
14	145	98.6	25	2	AAY42335	Aay42335 Omega-con
15	145	98.6	25	3	AAY56473	Aay56473 Natural o
16	145	98.6	25	3	AAY43714	Aay43714 Amino aci
17	145	98.6	25	3	AAB14352	Aab14352 Omega-con
18	145	98.6	25	4	AAB92219	Aab92219 Toxin pep
19	145	98.6	25	4	AAB19442	Aab19442 Primary s
20	145	98.6	25	4	AAB97046	Aab97046 Omega-con
21	145	98.6	25	5	AAO15124	Aao15124 Cone snai
22	145	98.6	26	2	AAR12546	Aar12546 Omega con
23	145	98.6	26	2	AAR37765	Aar37765 SNX-193.
24	145	98.6	26	2	AAW19557	Aaw19557 SNX-193,
25	145	98.6	26	3	AAY56485	Aay56485 Analogue
26	145	98.6	27	2	AAR13266	Aar13266 Omega con
27	145	98.6	27	2	AAR13265	Aar13265 Omega con
28	145	98.6	27	2	AAR37768	Aar37768 SNX-196.
29	145	98.6	27	2	AAR37769	Aar37769 SNX-197.
30	145	98.6	27	2	AAW19561	Aaw19561 SNX-197,
31	145	98.6	27	2	AAW19560	Aaw19560 SNX-196,
32	145	98.6	27	3	AAY56488	Aay56488 Analogue
33	145	98.6	27	3	AAY56489	Aay56489 Analogue
34	145	98.6	29	3	AAY84655	Aay84655 Amino aci
35	145	98.6	32	3	AAY84656	Aay84656 Amino aci
36	145	98.6	32	3	AAY84654	Aay84654 Amino aci
37	142	96.6	25	2	AAR12547	Aar12547 Omega con
38	142	96.6	25	4	AAB97043	Aab97043 Omega-con
39	141	95.9	25	4	AAB97044	Aab97044 Omega-con
40	141	95.9	25	4	AAB97045	Aab97045 Omega-con
41	140	95.2	25	2	AAW12983	Aaw12983 Omega con
42	140	95.2	25	2	AAW72623	Aaw72623 Conus gen
43	140	95.2	25	2	AAW95582	Aaw95582 Analog om
44	140	95.2	25	3	AAB14368	Aab14368 Omega-con
45	140	95.2	25	4	AAB19460	Aab19460 Sequence
46	139	94.6	25	2	AAR12544	Aar12544 Omega con
47	139	94.6	25	2	AAR13264	Aar13264 Omega con
48	139	94.6	25	2	AAR12545	Aar12545 Omega con
49	139	94.6	25	2	AAR39625	Aar39625 SNX-198.
50	139	94.6	25	2	AAR39618	Aar39618 SNX-190.

ALIGNMENTS

RESULT 1
AAR39626
ID AAR39626 standard; peptide; 25 AA.
XX
AC AAR39626;
XX
DT 25-MAR-2003 (revised)
DT 20-DEC-1993 (first entry)
XX
DE SNX-200.
XX
KW Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW narcotics.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /note= "Amidated C-terminal"
XX
PN WO9313128-A1.
XX
PD 08-JUL-1993.
XX
PF 30-DEC-1992; 92WO-US011349.
XX
PR 30-DEC-1991; 91US-00814759.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Justice A, Singh T, Gohil K, Valentino KL, Miljanich GP;
XX
DR WPI; 1993-227270/28.
XX
PT Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT pain etc.
XX

PS Claim 1; Fig 2; 90pp; English.
XX
CC The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC derivatives of these, which may be used to produce analgesia in a mammal.
CC These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC tissue. This is shown by the peptides ability to stimulate contraction in
CC guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC neuronal tissue. OCTs are components of peptide toxins derived from
CC marine snails of the genus Conus, and act as calcium channel blockers.
CC These OCTs may be used to replace opiods in the treatment of chronic pain
CC or to reduce the opiod dosage required. This helps to reduce dependence
CC on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC PN field.)
XX
SQ Sequence 25 AA;

Query Match 99.3%; Score 146; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 1.5e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||
Db 1 CKGKGAACSRLMYDCCTGSCRSGKC 25

RESULT 2
AAR37771
ID AAR37771 standard; peptide; 25 AA.
XX
AC AAR37771;
XX
DT 25-MAR-2003 (revised)
DT 08-SEP-1993 (first entry)
XX
DE SNX-200.
XX
KW Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW N-channel mediated neurotransmitter release.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9310145-A1.
XX
PD 27-MAY-1993.
XX
PF 12-NOV-1992; 92WO-US009766.
XX
PR 12-NOV-1991; 91US-00789913.
PR 17-JUL-1992; 92US-00916478.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bowersox SS, Fox JA, Valentino KL, Bitner RS;
PI Yamashiro DH;
XX
DR WPI; 1993-182487/22.
XX
PT Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS Disclosure; Fig 2; 103pp; English.
XX
CC The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC 207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC delaying admin. for some time (compare US5051403 where cpds. are given
CC within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC treatment with antihistamines to minimise redn. in blood pressure caused
CC by (I)). (I) is also at least as effective as the specified conotoxins
CC for (1) selective inhibition of N-type voltage-gated Ca currents in
CC neuronal tissue and (2) selective inhibition of N-channel mediated
CC neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 25 AA;

Query Match 99.3%; Score 146; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 1.5e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||
Db 1 CKGKGAACSRLMYDCCTGSCRSGKC 25

RESULT 3
AAW19564
ID AAW19564 standard; peptide; 25 AA.
XX
AC AAW19564;
XX
DT 14-OCT-1997 (first entry)
XX
DE SNX-200, omega conopeptide derivative used for pain relief.
XX
KW Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW N-type voltage-sensitive calcium channel; block; Conus.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /note= "amidated"
XX
PN WO9701351-A1.
XX
PD 16-JAN-1997.
XX
PF 26-JUN-1996; 96WO-US011041.
XX
PR 27-JUN-1995; 95US-00496847.
PR 08-MAR-1996; 96US-00613400.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Amstutz GA, Bowersox SS, Gohil K, Adriaenssens PI, Kristipati R;
PI Gadbois T, Pettus MR, Luther RR;
XX
DR WPI; 1997-100012/09.
XX
PT Stable omega conopeptide compositions - for producing analgesia and for
PT inhibiting progression of neuropathic pain disorders.
XX
PS Disclosure; Fig 3; 47pp; English.
XX
CC AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC peptides from Conus sp. (cone snails). The peptides and their analogues
CC are used as analgesics acting by blocking N-type voltage-sensitive
CC calcium channels. The OCs can be used to treat neuropathic pain as a

CC result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC hyperalgesia. The OCs are preferably administered in a medicament via an
CC epidural route in a continuous infusion or sustained release formulation.
CC The OCs can provide pain relief when administered epidurally in the
CC absence of a permeation enhancer, at doses that are comparable to
CC effective analgesic doses using intrathecal administration. OC
CC formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC They also confer stability to solutions containing them for prolonged
CC treatment methods and long-term storage
XX
SQ Sequence 25 AA;

Query Match 99.3%; Score 146; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 1.5e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
|||||| ||||||||||||||||||||
Db 1 CKGKGAACSRLMYDCCTGSCRSGKC 25

RESULT 4
AAY56492
ID AAY56492 standard; peptide; 25 AA.
XX
AC AAY56492;
XX
DT 16-FEB-2000 (first entry)
XX
DE Analogue omega conopeptide SNX-200.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /note= "amidated"
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 2; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 25 AA;

Query Match 99.3%; Score 146; DB 3; Length 25;
Best Local Similarity 96.0%; Pred. No. 1.5e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
|||||| ||||||||||||||||||||
Db 1 CKGKGAACSRLMYDCCTGSCRSGKC 25

RESULT 5
AAR39608
ID AAR39608 standard; peptide; 25 AA.
XX
AC AAR39608;
XX
DT 25-MAR-2003 (revised)
DT 20-DEC-1993 (first entry)
XX
DE MVIIA/SNX111.
XX
KW Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW narcotics.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9313128-A1.
XX
PD 08-JUL-1993.
XX
PF 30-DEC-1992; 92WO-US011349.
XX
PR 30-DEC-1991; 91US-00814759.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Justice A, Singh T, Gohil K, Valentino KL, Miljanich GP;
XX
DR WPI; 1993-227270/28.
XX
PT Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT pain etc.
XX
PS Claim 1; Fig 1; 90pp; English.
XX
CC The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC derivatives of these, which may be used to produce analgesia in a mammal.
CC These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC tissue. This is shown by the peptides ability to stimulate contraction in
CC guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC neuronal tissue. OCTs are components of peptide toxins derived from
CC marine snails of the genus Conus, and act as calcium channel blockers.
CC These OCTs may be used to replace opiods in the treatment of chronic pain

```
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 6
AAR37752
ID   AAR37752 standard; peptide; 25 AA.
XX
AC   AAR37752;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   MVIIA/SNX-111.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 1; 103pp; English.
XX
CC   Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC   hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC   omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC   at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC   that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC   or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC   damage caused by stroke. By delaying admin. for some time (compare
CC   US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC   greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC   intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC   be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC   in blood pressure caused by (I)). (I) is also at least as effective as
CC   the specified conotoxins for (1) selective inhibition of N-type voltage-
CC   gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC   channel mediated neurotransmitter release in neuronal tissue. Primary
CC   sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC   omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC   correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 7
AAR32777
ID   AAR32777 standard; peptide; 25 AA.
XX
AC   AAR32777;
XX
DT   28-JUN-1993  (first entry)
XX
DE   MVIIA omega conotoxin peptide.
XX
KW   OCT; neuronal damage reduction; ischemia; secondary damage; stroke.
XX
OS   Synthetic.
XX
PN   US5189020-A.
XX
PD   23-FEB-1993.
XX
PF   02-AUG-1990;   90US-00561766.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH,  Tsubokawa M;
XX
DR   WPI; 1993-085564/10.
XX
PT   Reducing neuronal damage due to ischaemia - involves using omega
PT   conotoxin peptide or fragment.
XX
PS   Disclosure; Fig 1; 32pp; English.
XX
CC   The sequence is that of the MVIIA omega conotoxin (OCT) peptide which can
CC   bind to an OCT binding protein, inhibit voltage-gated calcium currents
CC   selectively in neuronal tissue and inhibit neuronal transmitter release
CC   selectively in neuronal tissue. These properties all occur within the
CC   range of those of MVIIB, GVIIA, RVIA, or pref. MVIIA and GVIA OCTs. The
CC   peptide can be used in reducing or preventing both anatomical and
CC   functional secondary damage related to ischemia, generally as associated
CC   with stroke
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 8
AAR76089
ID   AAR76089 standard; peptide; 25 AA.
```

```
XX
AC   AAR76089;
XX
DT   27-AUG-2003  (revised)
DT   25-MAR-2003  (revised)
DT   02-FEB-1996  (first entry)
XX
DE   Omega conotoxin MVIIA peptide.
XX
KW   Omega conotoxin; marine snail; Conus; voltage-gated Ca channel blocker;
KW   synaptosome; membrane; fish electric organ; mammalian brain; ischaemia;
KW   binding protein; binding affinity; stroke.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "amidated C-terminus"
XX
PN   US5424218-A.
XX
PD   13-JUN-1995.
XX
PF   04-NOV-1993;   93US-00147714.
XX
PR   22-NOV-1989;   89US-00440094.
PR   02-AUG-1990;   90US-00561766.
PR   23-MAR-1992;   92US-00855269.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Valentino KL,  Bowersox SS,  Bitner RS,  Miljanich GP,  Yamashiro DH;
PI   Fox JA;
XX
DR   WPI; 1995-223694/29.
XX
PT   Identifying cpds. able to reduce neuronal damage caused by ischaemia - by
PT   measuring their affinity to omega conotoxin MVIIA binding site and
PT   ability e.g. to inhibit voltage gated calcium channels.
XX
PS   Disclosure; Fig 1; 31pp; English.
XX
CC   The peptides AAR76089-95 are naturally occuring omega conotoxin (OCT)
CC   peptides derived from marine snails of the Conus genus. The peptide
CC   sequences were used to chemically synthesise the OCT peptide fragments
CC   AAR76096-R76109. The OCT peptides act as voltage-gated Ca channel
CC   blockers by binding to a 210 kD protein from synaptosomal membrane
CC   preparations from fish electric organ or mammalian brains. The peptides
CC   and their synthesised fragments can be used to screen for compounds that
CC   bind to the OCT binding protein, by displacing a high affinity labelled
CC   OCT, such as MVIIA, from a synaptosomal membrane preparation. The
CC   compounds should have binding affinities and activities at least equal to
CC   those of the natural peptides (Ki 0.44-324 nM). The screened compounds
CC   are potentially useful in treating ischaemic conditions, esp. stroke, and
CC   can reduce sec. anatomical and functional damage associated with those
CC   conditions. (Updated on 25-MAR-2003 to correct PF field.) (Updated on 27-
CC   AUG-2003 to correct OS field.)
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 9
AAW19544
ID   AAW19544 standard; peptide; 25 AA.
XX
AC   AAW19544;
XX
DT   27-AUG-2003  (revised)
DT   13-OCT-1997  (first entry)
XX
DE   Natural omega-conopeptide MVIIA/SNX-111 used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Conus.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "optionally amidated"
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Claim 3; Fig 1, Fig 3; 47pp; English.
XX
CC   AAW19544-W19553 are naturally occurring omega conopeptides (OCs) isolated
CC   from Conus sp. (cone snails). The peptides and their analogues are used
CC   as analgesics acting by blocking N-type voltage-sensitive calcium
CC   channels. The OCs can be used to treat neuropathic pain as a result of
CC   e.g. insult to the spinal cord or peripheral nerves, cancer, bone
CC   degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes zoster
CC   neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage. (Updated on 27-AUG-2003 to
CC   correct OS field.)
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 10
AAW19569
```

```
ID   AAW19569 standard; peptide; 25 AA.
XX
AC   AAW19569;
XX
DT   14-OCT-1997  (first entry)
XX
DE   SNX-279, omega conopeptide derivative used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Misc-difference 12
FT                   /label= Met(O)
FT                   /note= "sulphoxymethionine"
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "amidated"
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Claim 3; Fig 3; 47pp; English.
XX
CC   AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC   peptides from Conus sp. (cone snails). The peptides and their analogues
CC   are used as analgesics acting by blocking N-type voltage-sensitive
CC   calcium channels. The OCs can be used to treat neuropathic pain as a
CC   result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC   bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC   zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 11
AAW12967
ID   AAW12967 standard; peptide; 25 AA.
XX
AC   AAW12967;
XX
DT   25-MAR-2003  (revised)
DT   22-APR-1997  (first entry)
XX
DE   Omega conopeptide SNX-111.
XX
KW   Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW   neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW   acute dystonic reactions; inflammation; epilepsy.
XX
OS   Synthetic.
XX
PN   US5587454-A.
XX
PD   24-DEC-1996.
XX
PF   15-APR-1993;   93US-00049794.
XX
PR   30-DEC-1991;   91US-00814759.
PR   30-DEC-1992;   92WO-US011349.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Gohil KC,  Miljanich GP,  Valentino KL,  Justice A,  Singh T;
XX
DR   WPI; 1997-064830/06.
XX
PT   Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT   neuropathic pain.
XX
PS   Example 1; Col 39-40; 58pp; English.
XX
CC   The present peptide is an omega conopeptide, useful as an analgesic,
CC   especially for treating neuropathic pain. The peptide, which can be
CC   prepared by solid phase synthesis, can also be used to inhibit neuronal
CC   damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC   reactions, inflammation and epilepsy. In a rat paw formalin test, the
CC   peptide had an ED50 of 0.011 microg in phase 1, and 0.011 microg in phase
CC   2 (by intrathecal administration). (Updated on 25-MAR-2003 to correct PF
CC   field.)
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 12
AAW72605
ID   AAW72605 standard; peptide; 25 AA.
XX
AC   AAW72605;
XX
DT   27-AUG-2003  (revised)
DT   06-JAN-1999  (first entry)
XX
DE   Conus genus natural omega-conopeptide MVIIA/SNX-111.
XX
KW   Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW   nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW   inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
KW   rheumatoid arthritis; epilepsy.
XX
OS   Conus.
XX
```

PN US5824645-A.
XX
PD 20-OCT-1998.
XX
PF 01-NOV-1996; 96US-00742774.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Valentino KL, Gohil KC, Justice A, Singh T;
XX
DR WPI; 1998-582596/49.
XX
PT Treatment of inflammation, comprises administration of omega-conopeptide
PT - effective to block voltage-gated calcium channels, bind with high
PT affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT release.
XX
PS Disclosure; Fig 1; 58pp; English.
XX
CC A method has been developed for the treatment of inflammation in a
CC subject. The method comprises administration of an omega-conopeptide
CC effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC neurotransmitter release from nervous tissue. The method is used to treat
CC inflammation and associated pain. The treatment can also be used to
CC produce analgesia (especially in subjects experiencing neuropathic pain);
CC and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC represents a natural omega-conopeptide. Omega-conopeptides are components
CC of peptide toxins produced by marine snails of the genus Conus, and which
CC act as calcium channel blockers. (Updated on 27-AUG-2003 to correct OS
CC field.)
XX
SQ Sequence 25 AA;

Query Match 98.6%; Score 145; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 2e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 13
AAW95564
ID AAW95564 standard; protein; 25 AA.
XX
AC AAW95564;
XX
DT 29-MAR-1999 (first entry)
XX
DE Omega-conopeptide MVIIA/SNX-111.
XX
KW Omega-conopeptide; peptide toxin; snail; calcium channel blocker;
KW analgesia; guinea pig ileum; omega-conotoxin; pain; neuropathic.
XX
OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Modified-site 25
FT /note= "C-terminal amide"
XX
PN US5859186-A.
XX
PD 12-JAN-1999.
XX
PF 03-JUL-1996; 96US-00675354.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Gohil KC, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1999-120002/10.
XX
PT Production of analgesia in mammal - by administration of omega cono-
PT peptide(s).
XX
PS Claim 3; Fig 1; 59pp; English.
XX
CC Sequences AAW95564-573 represent primary sequences of natural omega-
CC conopeptides. Omega-conopeptides are components of peptide toxins
CC produced by marine snails of the genus Conus, and which act as calcium
CC channel blockers. The invention relates to a method of producing
CC analgesia in a mammal that comprises administering an omega conopeptide
CC having activities in (a) inhibiting electrically stimulated contraction
CC of guinea pig ileum and (b) selectively binding to omega conopeptide
CC MVIIA binding sites in neuronal tissue, where these activities are within
CC the ranges of those of omega-conotoxins MVIIA and TVIA. The method is
CC used for treating chronic pain, especially neuropathic pain. The present
CC sequence is a specifically claimed example of an omega-conopeptide that
CC can be used in the method of the invention
XX
SQ Sequence 25 AA;

Query Match 98.6%; Score 145; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 2e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 14
AAY42335
ID AAY42335 standard; peptide; 25 AA.
XX
AC AAY42335;
XX
DT 20-DEC-1999 (first entry)
XX
DE Omega-conotoxin OCT MVIIA.
XX
KW Calcium channel; neuron; retina; optic nerve; trauma; ischaemia; vision;
KW prevention.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Misc-difference 25
FT /note= "Optionally contains C-terminal amide"
XX
PN US5965534-A.
XX
PD 12-OCT-1999.
XX
PF 13-MAR-1998; 98US-00039168.
XX
PR 22-NOV-1995; 95US-00562142.
XX
PA (ALCO-) ALCON LAB INC.
XX
PI Hellberg M, Pang I, Kapin M;
XX

DR WPI; 1999-579926/49.
XX
PT Treatment or prevention of retinal or optic nerve head damage comprises
PT administration of an omega-conotoxin derivative.
XX
PS Claim 2; Col 3-4; 7pp; English.
XX
CC This sequence represents omega-conotoxin OCT MVIIA. Omega-conotoxins
CC selectively block N-type calcium channels responsible for calcium influx
CC in neurons. Acute retinal or optic nerve damage, which can result in the
CC loss of vision, is caused by acute trauma and pathological events such as
CC ischaemia, hypoxia or oedema. The release of excitatory amino acids is
CC implicated in ischaemia-related neuronal and retinal damage, with
CC excitatory amino acid release leading to excessive stimulation of post-
CC synaptic excitatory amino acid receptors, which can result in cell
CC injury. The release of such excitatory amino acids from presynaptic nerve
CC terminals is dependent upon an elevation of calcium in the nerve
CC terminal. This presynaptic calcium influx is mediated by the N-type
CC calcium channels that are inhibited by omega-conotoxins. Intraocular
CC administration of at least one omega-conotoxin could be used for the
CC treatment or prevention of retinal or optic nerve head damage resulting
CC from acute traumatic or acute ischaemic events
XX
SQ Sequence 25 AA;

Query Match 98.6%; Score 145; DB 2; Length 25;
Best Local Similarity 96.0%; Pred. No. 2e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||| ||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 15
AAY56473
ID AAY56473 standard; peptide; 25 AA.
XX
AC AAY56473;
XX
DT 16-FEB-2000 (first entry)
XX
DE Natural omega conopeptide MVIIA/SNX-111.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 1; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 25 AA;

Query Match 98.6%; Score 145; DB 3; Length 25;
Best Local Similarity 96.0%; Pred. No. 2e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||| ||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 16
AAY43714
ID AAY43714 standard; peptide; 25 AA.
XX
AC AAY43714;
XX
DT 11-FEB-2000 (first entry)
XX
DE Amino acid sequence of an omega-conotoxin MVIIA(SNX-III).
XX
KW Omega-conotoxin; venom; predatory marine snail; N-type calcium channel;
KW neuronal damage reduction; ischemia; analgesia; opiate analgesia;
KW schizophrenia; stimulant induced psychosis; hypertension; inflammation;
KW bronchotension; neuropathic pain; voltage sensitive calcium channel.
XX
OS Conus magus.
XX
PN WO9954350-A1.
XX
PD 28-OCT-1999.
XX
PF 16-APR-1999; 99WO-AU000288.
XX
PR 16-APR-1998; 98AU-00002989.
PR 01-FEB-1999; 99AU-00008419.
XX
PA (UYQU) UNIV QUEENSLAND.
XX
PI Drinkwater RD, Lewis RJ, Alewood PF, Nielsen KJ;
XX
DR WPI; 2000-013226/01.
XX
PT Novel peptides used for the treatment of disorders and diseases where
PT blockage of the N-type calcium channels is required.
XX
PS Disclosure; Page 12; 81pp; English.
XX
CC The present sequence represents an omega-conotoxin. Omega-conotoxins are
CC isolated from venoms of predatory marine snails, and have a selectivity
CC for N-type calcium channels over P/Q type channels, and so block N-type
CC calcium channels. The omega-conotoxins of the invention can be used in
CC any disease or disorder where blockage of N-type calcium channels is
CC required, e.g. in the reduction of neuronal damage following ischemia,
CC production of analgesia, or enhancement of opiate analgesia, in the
CC treatment of schizophrenia, stimulant induced psychoses, hypertension,
CC inflammation, and diseases which cause bronchotension, and also in the
CC inhibition of progression of neuropathic pain. They can also be used in a

```
CC   screen to identify compounds with activity at N-type voltage sensitive
CC   calcium channels
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 17
AAB14352
ID   AAB14352 standard; peptide; 25 AA.
XX
AC   AAB14352;
XX
DT   06-DEC-2000  (first entry)
XX
DE   Omega-conopeptide MVIIA/SNX-111.
XX
KW   Marine snail; omega-conopeptide; calcium channel blocker; MVIIA; SNX-111;
KW   toxin; analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW   norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW   acute dystonic reaction; inflammation; epilepsy.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "C-terminal amide"
XX
PN   US6087091-A.
XX
PD   11-JUL-2000.
XX
PF   23-APR-1999;   99US-00298017.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2000-490177/43.
XX
PT   Selecting a compound for producing analgesia involves measuring activity
PT   of test compound in blocking voltage-gated calcium channels, binding to
PT   omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS   Example 1; Fig 1; 58pp; English.
XX
CC   The present sequence is an omega-conopeptide from marine snails of the
CC   genus Conus. Omega-conopeptides are components of peptide toxins produced
CC   by the cone snails, and which act as calcium channel blockers. Natural
CC   omega-conopeptides and their derivatives may be useful for producing
CC   analgesia in nociceptive and neuropathic pain. The peptides bind to omega
CC   -conopeptide binding sites, which are present mainly in neuronal tissue,
CC   and inhibit norepinephrine release from nervous tissue. Conopeptides such
CC   as MVIIA and TVIA are effective as therapeutic agents for treating
CC   neurogenic conditions such as schizophrenia, tardive dyskinesia and acute
CC   dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 18
AAB92219
ID   AAB92219 standard; peptide; 25 AA.
XX
AC   AAB92219;
XX
DT   22-JUN-2001  (first entry)
XX
DE   Toxin peptide SEQ ID NO:1395.
XX
KW   Protection; endogenous therapeutic peptide; peptidase; conjugation;
KW   blood component; modification; succinimidyl; maleimido group; amino;
KW   hydroxyl; thiol; hormone; growth factor; neurotransmitter.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO200069900-A2.
XX
PD   23-NOV-2000.
XX
PF   17-MAY-2000; 2000WO-US013576.
XX
PR   17-MAY-1999;   99US-0134406P.
PR   10-SEP-1999;   99US-0153406P.
PR   15-OCT-1999;   99US-0159783P.
XX
PA   (CONJ-) CONJUCHEM INC.
XX
PI   Bridon DP,  Ezrin AM,  Milner PG,  Holmes DL,  Thibaudeau K;
XX
DR   WPI; 2001-112059/12.
XX
PT   Modifying and attaching therapeutic peptides to albumin prevents
PT   peptidase degradation, useful for increasing length of in vivo activity.
XX
PS   Disclosure; Page 653; 733pp; English.
XX
CC   The present invention describes a modified therapeutic peptide (I)
CC   comprising a therapeutically active amino acid region (III) and a
CC   reactive group (II) (e.g. succinimidyl and maleimido groups) attached to
CC   a less therapeutically active amino acid region (IV), which covalently
CC   bonds with amino/hydroxyl/thiol groups on blood components to form a
CC   peptidase stabilised therapeutic peptide composed of 3-50 amino acids.
CC   (I) are useful for modifying therapeutic peptides e.g. hormones, growth
CC   factors and neurotransmitters, to protect them from peptidase activity in
CC   vivo for the treatment of various disorders. Endogenous therapeutic
CC   peptides are not suitable as drug candidates as they require frequent
CC   administration due to rapid degradation by peptidases in the body.
CC   Modifying and attaching therapeutic peptides to albumin prevents or
CC   reduces the action of peptidases to increase length of activity (half
CC   life) and specificity as bonding to large molecules decreases
CC   intracellular uptake and interference with physiological processes.
CC   AAB90829 to AAB92441 represent peptides which can be used in the
CC   exemplification of the present invention
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 4;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;
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Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 19
AAB19442
ID AAB19442 standard; peptide; 25 AA.
XX
AC AAB19442;
XX
DT 06-MAR-2001 (first entry)
XX
DE Primary sequence of a natural omega-conopeptide MVIIA/SNX-111.
XX
KW Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW epilepsy.
XX
OS Conus sp.
XX
FH Key   Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site   25
FT   /note= "amidated C-terminal"
XX
PN US6136786-A.
XX
PD 24-OCT-2000.
XX
PF 09-SEP-1999; 99US-00392979.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 23-JUN-1993; 93US-00081863.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
PR 23-APR-1999; 99US-00298017.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2001-030946/04.
XX
PT Enhancing analgesia produced by opiates by administering an omega-
PT conopeptide that inhibits electrically stimulated contraction of guinea
PT pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT tissues.
XX
PS Disclosure; Fig 1; 58pp; English.
XX
CC The present sequence represents an omega-conopeptide. Omega-conopeptides
CC are components of peptide toxins which act as voltage-gated calcium
CC channel inhibitors. The peptides are used to enhance the analgesic effect
CC produced by an opiate in a mammalian subject. The method comprises
CC administering to the subject an omega-conopeptide which is able to
CC inhibit electrically stimulated contraction of the guinea pig ileum and
CC bind to omega-conopeptide MVIIA binding sites present in neuronal tissue.
CC Omega-conopeptides are useful for enhancing the analgesic effect produced
CC by an opiate. Omega-conopeptides may also be used in the treatment of
CC pain, in reducing neuronal damage related to an ischemic condition in
CC mammals, and in treating schizophrenia, tardive dyskinesia and acute
CC dystonic reactions, inflammation and epilepsy
XX
SQ Sequence 25 AA;

```
  Query Match             98.6%;  Score 145;  DB 4;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 20
AAB97046
ID AAB97046 standard; peptide; 25 AA.
XX
AC AAB97046;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Disclosure; Page 10 (disclosure); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

```
  Query Match             98.6%;  Score 145;  DB 4;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 21
AAO15124
ID AAO15124 standard; peptide; 25 AA.
XX
AC AAO15124;
XX
DT 22-AUG-2002 (first entry)
XX
DE Cone snail w-conotoxin peptide MVIIA.
XX
KW Cone snail; venomous saliva; calcium channel blocking activity;
KW stenocardia; hypertension; myocarditis; arrhythmia; cerebral ischaemia;
KW w-conotoxin.

```
XX
OS   Conus sp.
XX
PN   JP2002080499-A.
XX
PD   19-MAR-2002.
XX
PF   01-SEP-2000; 2000JP-00266187.
XX
PR   01-SEP-2000; 2000JP-00266187.
XX
PA   (SUNR ) SUNTORY LTD.
XX
DR   WPI; 2002-421068/45.
XX
PT   A new peptide derived from venomous saliva of assassin bug, has calcium
PT   channel blocking activity.
XX
PS   Disclosure; Page 4; 26pp; Japanese.
XX
CC   The invention comprises peptides having calcium channel blocking
CC   activities which are derived from the venomous saliva of assassin bugs.
CC   The calcium channel blocking peptides of the invention are useful for
CC   treating stenocardia, hypertension, myocarditis, arrhythmia and cerebral
CC   ischaemia. The present amino acid sequence represents a cone snail w-
CC   conotoxin peptide
XX
SQ   Sequence 25 AA;

  Query Match             98.6%;  Score 145;  DB 5;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 22
AAR12546
ID   AAR12546 standard; protein; 26 AA.
XX
AC   AAR12546;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(193).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(193) is an analogue of OCT peptide MVIIA in which a Gly residue is
CC   added to the C-terminus. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-5, AAR12547 and AAR13264-6
XX
SQ   Sequence 26 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 26;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 23
AAR37765
ID   AAR37765 standard; peptide; 26 AA.
XX
AC   AAR37765;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-193.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC   hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC   omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC   at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC   that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC   or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
```

CC damage caused by stroke. By delaying admin. for some time (compare
CC US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC in blood pressure caused by (I)). (I) is also at least as effective as
CC the specified conotoxins for (1) selective inhibition of N-type voltage-
CC gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC channel mediated neurotransmitter release in neuronal tissue. Primary
CC sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC correct PN field.)
XX
SQ Sequence 26 AA;

Query Match 98.6%; Score 145; DB 2; Length 26;
Best Local Similarity 96.0%; Pred. No. 2.1e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
|||||| ||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 24
AAW19557
ID AAW19557 standard; peptide; 26 AA.
XX
AC AAW19557;
XX
DT 14-OCT-1997 (first entry)
XX
DE SNX-193, omega conopeptide derivative used for pain relief.
XX
KW Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW N-type voltage-sensitive calcium channel; block; Conus.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9701351-A1.
XX
PD 16-JAN-1997.
XX
PF 26-JUN-1996; 96WO-US011041.
XX
PR 27-JUN-1995; 95US-00496847.
PR 08-MAR-1996; 96US-00613400.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Amstutz GA, Bowersox SS, Gohil K, Adriaenssens PI, Kristipati R;
PI Gadbois T, Pettus MR, Luther RR;
XX
DR WPI; 1997-100012/09.
XX
PT Stable omega conopeptide compositions - for producing analgesia and for
PT inhibiting progression of neuropathic pain disorders.
XX
PS Disclosure; Fig 3; 47pp; English.
XX
CC AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC peptides from Conus sp. (cone snails). The peptides and their analogues
CC are used as analgesics acting by blocking N-type voltage-sensitive
CC calcium channels. The OCs can be used to treat neuropathic pain as a
CC result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC hyperalgesia. The OCs are preferably administered in a medicament via an
CC epidural route in a continuous infusion or sustained release formulation.
CC The OCs can provide pain relief when administered epidurally in the
CC absence of a permeation enhancer, at doses that are comparable to
CC effective analgesic doses using intrathecal administration. OC
CC formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC They also confer stability to solutions containing them for prolonged
CC treatment methods and long-term storage
XX
SQ Sequence 26 AA;

Query Match 98.6%; Score 145; DB 2; Length 26;
Best Local Similarity 96.0%; Pred. No. 2.1e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
|||||| ||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 25
AAY56485
ID AAY56485 standard; peptide; 26 AA.
XX
AC AAY56485;
XX
DT 16-FEB-2000 (first entry)
XX
DE Analogue omega conopeptide SNX-193.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 2; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on

```
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 26 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 26;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 26
AAR13266
ID   AAR13266 standard; protein; 27 AA.
XX
AC   AAR13266;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(197).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(197) is an analogue of OCT peptide MVIIA in which an Asn-Ser
CC   dipeptide has been added to the N-terminus. residue replaces Lys at
CC   position 2. The analogue gave IC(50) for inhibition of adrenaline release
CC   and Ki values outside the ranges of those of OCT peptides MVIIA, GVIA,
CC   and/or TVIA. It is thus not a candidate for a neuroprotective compound.
CC   See also AAR12542-7, AAR13264-5
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 27
AAR13265
ID   AAR13265 standard; protein; 27 AA.
XX
AC   AAR13265;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(196).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(196) is an analogue of OCT peptide MVIIA in which an Asn residue is
CC   addede to the N-terminus and a Gly residue is added to the C-terminus.
CC   The analogue gave IC(50) for inhibition of adrenaline release and Ki
CC   values within the ranges of those of OCT peptides MVIIA, GVIA, and/or
CC   TVIA. It is thus a candidate for a neuroprotective compound. See also
CC   AAR12542-7, AAR13264 and AAR13266
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 28
AAR37768
ID   AAR37768 standard; peptide; 27 AA.
XX
AC   AAR37768;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-196.
```

```
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC   hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC   omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC   at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC   that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC   or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC   damage caused by stroke. By delaying admin. for some time (compare
CC   US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC   greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC   intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC   be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC   in blood pressure caused by (I)). (I) is also at least as effective as
CC   the specified conotoxins for (1) selective inhibition of N-type voltage-
CC   gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC   channel mediated neurotransmitter release in neuronal tissue. Primary
CC   sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC   omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC   correct PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 29
AAR37769
ID   AAR37769 standard; peptide; 27 AA.
XX
AC   AAR37769;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-197.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 30
AAW19561
ID   AAW19561 standard; peptide; 27 AA.
XX
AC   AAW19561;
XX
DT   14-OCT-1997  (first entry)
XX
```

```
DE   SNX-197, omega conopeptide derivative used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;    96WO-US011041.
XX
PR   27-JUN-1995;    95US-00496847.
PR   08-MAR-1996;    96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Disclosure; Fig 3; 47pp; English.
XX
CC   AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC   peptides from Conus sp. (cone snails). The peptides and their analogues
CC   are used as analgesics acting by blocking N-type voltage-sensitive
CC   calcium channels. The OCs can be used to treat neuropathic pain as a
CC   result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC   bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC   zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 31
AAW19560
ID   AAW19560 standard; peptide; 27 AA.
XX
AC   AAW19560;
XX
DT   14-OCT-1997  (first entry)
XX
DE   SNX-196, omega conopeptide derivative used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;    96WO-US011041.
XX
PR   27-JUN-1995;    95US-00496847.
PR   08-MAR-1996;    96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Disclosure; Fig 3; 47pp; English.
XX
CC   AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC   peptides from Conus sp. (cone snails). The peptides and their analogues
CC   are used as analgesics acting by blocking N-type voltage-sensitive
CC   calcium channels. The OCs can be used to treat neuropathic pain as a
CC   result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC   bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC   zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 2;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 32
AAY56488
ID   AAY56488 standard; peptide; 27 AA.
XX
AC   AAY56488;
XX
DT   16-FEB-2000  (first entry)
XX
DE   Analogue omega conopeptide SNX-196.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
```

```
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
PT   inflammation.
XX
PS   Disclosure; Fig 2; 47pp; English.
XX
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 33
AAY56489
ID   AAY56489 standard; peptide; 27 AA.
XX
AC   AAY56489;
XX
DT   16-FEB-2000  (first entry)
XX
DE   Analogue omega conopeptide SNX-197.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
PT   inflammation.
XX
PS   Disclosure; Fig 2; 47pp; English.
XX
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 27 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 27;
  Best Local Similarity   96.0%;  Pred. No. 2.1e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 34
AAY84655
ID   AAY84655 standard; peptide; 29 AA.
XX
AC   AAY84655;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
```

```
FT   Misc-difference 1. .29
FT                   /note= "peptide is cyclised via these residues"
FT   Peptide         1. .25
FT                   /note= "conotoxin"
FT   Peptide         26. .29
FT                   /note= "linker"
XX
PN   WO200015654-A1.
XX
PD   23-MAR-2000.
XX
PF   14-SEP-1999;   99WO-AU000769.
XX
PR   14-SEP-1998;   98AU-00005895.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Craik DJ,  Daly NL,  Nielsen KJ;
XX
DR   WPI; 2000-271376/23.
XX
PT   Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT   diseases in humans.
XX
PS   Claim 10; Page 31; 43pp; English.
XX
CC   AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC   cyclised peptides have improved properties, compared to their linear
CC   counterparts. These include resistance to cleavage by proteases, high
CC   chemical stability, improved biophysical properties, reduced side effects
CC   and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC   type calcium channels, and so may be useful in the treatment of
CC   neurological disorders such as acute and chronic pain, stroke, traumatic
CC   brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC   disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC   useful in the treatment of neuropsychiatric disorders such as
CC   schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC   syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC   to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC   can be also used as neuropharmacological probes. Antibodies raised
CC   against the peptides are useful as therapeutic or diagnostic agents, and
CC   can be used to screen for the peptides
XX
SQ   Sequence 29 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 29;
  Best Local Similarity   96.0%;  Pred. No. 2.2e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 35
AAY84656
ID   AAY84656 standard; peptide; 32 AA.
XX
AC   AAY84656;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
OS   Synthetic.
OS   Conus sp.
XX
```

```
FH   Key             Location/Qualifiers
FT   Misc-difference 1. .32
FT                   /note= "peptide is cyclised via these residues"
FT   Peptide         1. .4
FT                   /note= "linker"
FT   Peptide         5. .29
FT                   /note= "conotoxin"
FT   Peptide         30. .32
FT                   /note= "linker"
XX
PN   WO200015654-A1.
XX
PD   23-MAR-2000.
XX
PF   14-SEP-1999;   99WO-AU000769.
XX
PR   14-SEP-1998;   98AU-00005895.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Craik DJ,  Daly NL,  Nielsen KJ;
XX
DR   WPI; 2000-271376/23.
XX
PT   Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT   diseases in humans.
XX
PS   Claim 10; Page 31; 43pp; English.
XX
CC   AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC   cyclised peptides have improved properties, compared to their linear
CC   counterparts. These include resistance to cleavage by proteases, high
CC   chemical stability, improved biophysical properties, reduced side effects
CC   and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC   type calcium channels, and so may be useful in the treatment of
CC   neurological disorders such as acute and chronic pain, stroke, traumatic
CC   brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC   disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC   useful in the treatment of neuropsychiatric disorders such as
CC   schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC   syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC   to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC   can be also used as neuropharmacological probes. Antibodies raised
CC   against the peptides are useful as therapeutic or diagnostic agents, and
CC   can be used to screen for the peptides
XX
SQ   Sequence 32 AA;

  Query Match             98.6%;  Score 145;  DB 3;  Length 32;
  Best Local Similarity   96.0%;  Pred. No. 2.4e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||||
Db          5 CKGKGAKCSRLMYDCCTGSCRSGKC 29


RESULT 36
AAY84654
ID   AAY84654 standard; peptide; 32 AA.
XX
AC   AAY84654;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
```

OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Misc-difference 1. .32
FT /note= "peptide is cyclised via these residues"
FT Peptide 1. .26
FT /note= "conotoxin"
FT Peptide 26. .32
FT /note= "linker"
XX
PN WO200015654-A1.
XX
PD 23-MAR-2000.
XX
PF 14-SEP-1999; 99WO-AU000769.
XX
PR 14-SEP-1998; 98AU-00005895.
XX
PA (UYQU) UNIV QUEENSLAND.
XX
PI Craik DJ, Daly NL, Nielsen KJ;
XX
DR WPI; 2000-271376/23.
XX
PT Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT diseases in humans.
XX
PS Claim 10; Page 31; 43pp; English.
XX
CC AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC cyclised peptides have improved properties, compared to their linear
CC counterparts. These include resistance to cleavage by proteases, high
CC chemical stability, improved biophysical properties, reduced side effects
CC and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC type calcium channels, and so may be useful in the treatment of
CC neurological disorders such as acute and chronic pain, stroke, traumatic
CC brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC useful in the treatment of neuropsychiatric disorders such as
CC schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC can be also used as neuropharmacological probes. Antibodies raised
CC against the peptides are useful as therapeutic or diagnostic agents, and
CC can be used to screen for the peptides
XX
SQ Sequence 32 AA;

Query Match 98.6%; Score 145; DB 3; Length 32;
Best Local Similarity 96.0%; Pred. No. 2.4e-09;
Matches 24; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

```
Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 37
AAR12547
ID AAR12547 standard; protein; 25 AA.
XX
AC AAR12547;
XX
DT 05-SEP-1991 (first entry)
XX
DE Omega conotoxin peptide analogue MVIIA(194).
XX
KW neuronal calcium-channel antagonist; OCT; adrenaline release;
KW neuroprotective.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Misc-difference 12
FT /label= Nle
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /label= amidated carboxy terminal
XX
PN WO9107980-A.
XX
PD 13-JUN-1991.
XX
PF 22-NOV-1989; 89US-00440094.
XX
PR 22-NOV-1989; 89US-00440094.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanjich GP, Bitner RS, Bowersox SS, Fox JA, Valentino KL;
PI Yamashiro DH;
XX
DR WPI; 1991-192969/26.
XX
PT Compsn. for reducing ischaemia-related neuronal damage - contains
PT neuronal channel antagonist omega conotoxin peptide which blocks
PT norepinephrine release in central nervous system neuronal cells.
XX
PS Disclosure; Fig 2; 74pp; English.
XX
CC MVIIA(194) is an analogue of OCT peptide MVIIA in which a Nle residue
CC replaces Met at position 12. The analogue gave IC(50) for inhibition of
CC adrenaline release and Ki values within the ranges of those of OCT
CC peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC neuroprotective compound. See also AAR12542-6 and AAR13264-6
XX
SQ Sequence 25 AA;

Query Match 96.6%; Score 142; DB 2; Length 25;
Best Local Similarity 92.0%; Pred. No. 4.3e-09;
Matches 23; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| |||||:|||||||||||||
Db          1 CKGKGAKCSRLLYDCCTGSCRSGKC 25
```

RESULT 38
AAB97043
ID AAB97043 standard; peptide; 25 AA.
XX
AC AAB97043;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA variant polypeptide #3.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX

DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 3; Page 1 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 96.6%; Score 142; DB 4; Length 25;
Best Local Similarity 92.0%; Pred. No. 4.3e-09;
Matches 23; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||:||||:|||||||||||||
Db 1 CKGKGAKCSRLLYDCCTGSCRSGKC 25

RESULT 39
AAB97044
ID AAB97044 standard; peptide; 25 AA.
XX
AC AAB97044;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA variant polypeptide #4.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 4; Page 1 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 95.9%; Score 141; DB 4; Length 25;
Best Local Similarity 92.0%; Pred. No. 5.6e-09;
Matches 23; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||:||||:|||||||||||||
Db 1 CKGKGAKCSRLIYDCCTGSCRSGKC 25

RESULT 40
AAB97045
ID AAB97045 standard; peptide; 25 AA.
XX
AC AAB97045;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA variant polypeptide #5.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 5; Page 2 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 95.9%; Score 141; DB 4; Length 25;
Best Local Similarity 92.0%; Pred. No. 5.6e-09;
Matches 23; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||||||:||||:|||||||||||||
Db 1 CKGKGAKCSRLVYDCCTGSCRSGKC 25

RESULT 41
AAW12983
ID AAW12983 standard; peptide; 25 AA.
XX
AC AAW12983;
XX
DT 25-MAR-2003 (revised)
DT 22-APR-1997 (first entry)
XX
DE Omega conopeptide SNX-200.
XX
KW Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW neuronal damage; schizophrenia; tardive dyskinesia; analgesia;

KW acute dystonic reactions; inflammation; epilepsy.
XX
OS Synthetic.
XX
PN US5587454-A.
XX
PD 24-DEC-1996.
XX
PF 15-APR-1993; 93US-00049794.
XX
PR 30-DEC-1991; 91US-00814759.
PR 30-DEC-1992; 92WO-US011349.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Gohil KC, Miljanich GP, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1997-064830/06.
XX
PT Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT neuropathic pain.
XX
PS Disclosure; Col 51-52; 58pp; English.
XX
CC The present peptide is an omega conopeptide, useful as an analgesic,
CC especially for treating neuropathic pain. The peptide, which can be
CC prepared by solid phase synthesis, can also be used to inhibit neuronal
CC damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC reactions, inflammation and epilepsy. (Updated on 25-MAR-2003 to correct
CC PF field.)
XX
SQ Sequence 25 AA;

Query Match 95.2%; Score 140; DB 2; Length 25;
Best Local Similarity 92.0%; Pred. No. 7.2e-09;
Matches 23; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||| || ||||||||||||||||||||
Db 1 CKGAGAACSRLMYDCCTGSCRSGKC 25

RESULT 42
AAW72623
ID AAW72623 standard; peptide; 25 AA.
XX
AC AAW72623;
XX
DT 27-AUG-2003 (revised)
DT 06-JAN-1999 (first entry)
XX
DE Conus genus analogue omega-conopeptide SNX-200.
XX
KW Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
KW rheumatoid arthritis; epilepsy.
XX
OS Conus.
XX
PN US5824645-A.
XX
PD 20-OCT-1998.
XX
PF 01-NOV-1996; 96US-00742774.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Valentino KL, Gohil KC, Justice A, Singh T;
XX
DR WPI; 1998-582596/49.
XX
PT Treatment of inflammation, comprises administration of omega-conopeptide
PT - effective to block voltage-gated calcium channels, bind with high
PT affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT release.
XX
PS Disclosure; Fig 2; 58pp; English.
XX
CC A method has been developed for the treatment of inflammation in a
CC subject. The method comprises administration of an omega-conopeptide
CC effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC neurotransmitter release from nervous tissue. The method is used to treat
CC inflammation and associated pain. The treatment can also be used to
CC produce analgesia (especially in subjects experiencing neuropathic pain);
CC and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC represents an analogue omega-conopeptide. Omega-conopeptides are
CC components of peptide toxins produced by marine snails of the genus
CC Conus, and which act as calcium channel blockers. (Updated on 27-AUG-2003
CC to correct OS field.)
XX
SQ Sequence 25 AA;

Query Match 95.2%; Score 140; DB 2; Length 25;
Best Local Similarity 92.0%; Pred. No. 7.2e-09;
Matches 23; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||| || ||||||||||||||||||||
Db 1 CKGAGAACSRLMYDCCTGSCRSGKC 25

RESULT 43
AAW95582
ID AAW95582 standard; protein; 25 AA.
XX
AC AAW95582;
XX
DT 29-MAR-1999 (first entry)
XX
DE Analog omega-conopeptide SNX-200.
XX
KW Omega-conopeptide; peptide toxin; snail; calcium channel blocker;
KW analgesia; guinea pig ileum; omega-conotoxin; pain; neuropathic.
XX
OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Modified-site 25
FT /note= "C-terminal amide"
XX
PN US5859186-A.
XX
PD 12-JAN-1999.
XX
PF 03-JUL-1996; 96US-00675354.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Gohil KC, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1999-120002/10.
XX
PT Production of analgesia in mammal - by administration of omega cono-
PT peptide(s).
XX

PS Disclosure; Fig 2A-B; 59pp; English.
XX
CC Sequences AAW95574-589 represent sequences of analog omega-conopeptides.
CC Omega-conopeptides are components of peptide toxins produced by marine
CC snails of the genus Conus, and which act as calcium channel blockers. The
CC invention relates to a method of producing analgesia in a mammal that
CC comprises administering an omega conopeptide having activities in (a)
CC inhibiting electrically stimulated contraction of guinea pig ileum and
CC (b) selectively binding to omega conopeptide MVIIA binding sites in
CC neuronal tissue, where these activities are within the ranges of those of
CC omega-conotoxins MVIIA and TVIA. The method is used for treating chronic
CC pain, especially neuropathic pain
XX
SQ Sequence 25 AA;

Query Match 95.2%; Score 140; DB 2; Length 25;
Best Local Similarity 92.0%; Pred. No. 7.2e-09;
Matches 23; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||| || ||||||||||||||||||||
Db 1 CKGAGAACSRLMYDCCTGSCRSGKC 25

RESULT 44
AAB14368
ID AAB14368 standard; peptide; 25 AA.
XX
AC AAB14368;
XX
DT 06-DEC-2000 (first entry)
XX
DE Omega-conopeptide SNX-200.
XX
KW Marine snail; omega-conopeptide; calcium channel blocker; SNX-200; toxin;
KW analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW acute dystonic reaction; inflammation; epilepsy.
XX
OS Conus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /note= "C-terminal amide"
XX
PN US6087091-A.
XX
PD 11-JUL-2000.
XX
PF 23-APR-1999; 99US-00298017.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2000-490177/43.
XX
PT Selecting a compound for producing analgesia involves measuring activity
PT of test compound in blocking voltage-gated calcium channels, binding to
PT omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS Disclosure; Fig 2; 58pp; English.
XX
CC The present sequence is an omega-conopeptide analogue. Omega-conopeptides
CC are components of peptide toxins produced marine snails of the genus
CC Conus. Omega-conopeptides and their derivatives act as calcium channel
CC blockers and may be useful for producing analgesia in nociceptive and
CC neuropathic pain. The peptides bind to omega-conopeptide binding sites,
CC which are present mainly in neuronal tissue, and inhibit norepinephrine
CC release from nervous tissue. Conopeptides such as MVIIA and TVIA are
CC effective as therapeutic agents for treating neurogenic conditions such
CC as schizophrenia, tardive dyskinesia and acute dystonic reactions,
CC inflammation and epilepsy
XX
SQ Sequence 25 AA;

Query Match 95.2%; Score 140; DB 3; Length 25;
Best Local Similarity 92.0%; Pred. No. 7.2e-09;
Matches 23; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

Qy 1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
||| || ||||||||||||||||||||
Db 1 CKGAGAACSRLMYDCCTGSCRSGKC 25

RESULT 45
AAB19460
ID AAB19460 standard; peptide; 25 AA.
XX
AC AAB19460;
XX
DT 06-MAR-2001 (first entry)
XX
DE Sequence of an omega-conopeptide analogue designated SNX-200.
XX
KW Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW epilepsy.
XX
OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Modified-site 25
FT /note= "amidated residue"
XX
PN US6136786-A.
XX
PD 24-OCT-2000.
XX
PF 09-SEP-1999; 99US-00392979.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 23-JUN-1993; 93US-00081863.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
PR 23-APR-1999; 99US-00298017.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2001-030946/04.
XX
PT Enhancing analgesia produced by opiates by administering an omega-
PT conopeptide that inhibits electrically stimulated contraction of guinea
PT pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT tissues.
XX
PS Disclosure; Col 51-52; 58pp; English.
XX
CC The present sequence represents an omega-conopeptide analogue. Omega-
CC conopeptides are components of peptide toxins which act as voltage-gated

```
CC   calcium channel inhibitors. The peptides are used to enhance the
CC   analgesic effect produced by an opiate in a mammalian subject. The method
CC   comprises administering to the subject an omega-conopeptide which is able
CC   to inhibit electrically stimulated contraction of the guinea pig ileum
CC   and bind to omega-conopeptide MVIIA binding sites present in neuronal
CC   tissue. Omega-conopeptides are useful for enhancing the analgesic effect
CC   produced by an opiate. Omega-conopeptides may also be used in the
CC   treatment of pain, in reducing neuronal damage related to an ischemic
CC   condition in mammals, and in treating schizophrenia, tardive dyskinesia
CC   and acute dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 25 AA;

  Query Match             95.2%;  Score 140;  DB 4;  Length 25;
  Best Local Similarity   92.0%;  Pred. No. 7.2e-09;
  Matches   23;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              ||| || ||||||||||||||||||
Db          1 CKGAGAACSRLMYDCCTGSCRSGKC 25


RESULT 46
AAR12544
ID   AAR12544 standard; protein; 25 AA.
XX
AC   AAR12544;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(190).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(190) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 4. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-3, AAR12545-7 and AAR13264-6
XX
SQ   Sequence 25 AA;

  Query Match             94.6%;  Score 139;  DB 2;  Length 25;
  Best Local Similarity   92.0%;  Pred. No. 9.3e-09;
  Matches   23;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              ||| || ||||||||||||||||||
Db          1 CKGAGAKCSRLMYDCCTGSCRSGKC 25


RESULT 47
AAR13264
ID   AAR13264 standard; protein; 25 AA.
XX
AC   AAR13264;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(195).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(195) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 24. The analogue gave a Ki value within the
CC   ranges of those of OCT peptides MVIIA, GVIA, and/or TVIA. It gave an
CC   IC(50) for inhibition of adrenaline release outside the range for these
CC   neuroprotective compounds. See also AAR12542-7, and AAR13265-6
XX
SQ   Sequence 25 AA;

  Query Match             94.6%;  Score 139;  DB 2;  Length 25;
  Best Local Similarity   92.0%;  Pred. No. 9.3e-09;
  Matches   23;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| |||||||||||||||| |
Db          1 CKGKGAKCSRLMYDCCTGSCRSGAC 25


RESULT 48
AAR12545
ID   AAR12545 standard; protein; 25 AA.
XX
```

```
AC   AAR12545;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(191).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(191) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 2. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-4, AAR12546-7 and AAR13264-6
XX
SQ   Sequence 25 AA;

  Query Match             94.6%;  Score 139;  DB 2;  Length 25;
  Best Local Similarity   92.0%;  Pred. No. 9.3e-09;
  Matches   23;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              | |||| ||||||||||||||||||
Db          1 CAGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 49
AAR39625
ID   AAR39625 standard; peptide; 25 AA.
XX
AC   AAR39625;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-198.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             94.6%;  Score 139;  DB 2;  Length 25;
  Best Local Similarity   92.0%;  Pred. No. 9.3e-09;
  Matches   23;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||| ||||
Db          1 CKGKGAKCSRLMYDCCTGSCASGKC 25


RESULT 50
AAR39618
ID   AAR39618 standard; peptide; 25 AA.
XX
AC   AAR39618;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-190.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
```

FT Modified-site 25
FT /note= "Amidated C-terminal"
XX
PN WO9313128-A1.
XX
PD 08-JUL-1993.
XX
PF 30-DEC-1992; 92WO-US011349.
XX
PR 30-DEC-1991; 91US-00814759.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Justice A, Singh T, Gohil K, Valentino KL, Miljanich GP;
XX
DR WPI; 1993-227270/28.
XX
PT Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT pain etc.
XX
PS Claim 1; Fig 2; 90pp; English.
XX
CC The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC derivatives of these, which may be used to produce analgesia in a mammal.
CC These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC tissue. This is shown by the peptides ability to stimulate contraction in
CC guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC neuronal tissue. OCTs are components of peptide toxins derived from
CC marine snails of the genus Conus, and act as calcium channel blockers.
CC These OCTs may be used to replace opiods in the treatment of chronic pain
CC or to reduce the opiod dosage required. This helps to reduce dependence
CC on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC PN field.)
XX
SQ Sequence 25 AA;

Query Match 94.6%; Score 139; DB 2; Length 25;
Best Local Similarity 92.0%; Pred. No. 9.3e-09;
Matches 23; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

```
Qy          1 CKGKGAXCSRLMYDCCTGSCRSGKC 25
              ||| || |||||||||||||||||||
Db          1 CKGAGAKCSRLMYDCCTGSCRSGKC 25
```

Search completed: March 28, 2005, 16:39:26
Job time : 66.6667 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 28, 2005, 16:30:33 ; Search time 66.6667 Seconds
(without alignments)
145.035 Million cell updates/sec

Title: US-09-787-082A-10
Perfect score: 151
Sequence: 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 50 summaries

Database : A_Geneseq_16Dec04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	151	100.0	25	2	AAR39608	Aar39608 MVIIA/SNX
2	151	100.0	25	2	AAR37752	Aar37752 MVIIA/SNX
3	151	100.0	25	2	AAR32777	Aar32777 MVIIA ome
4	151	100.0	25	2	AAR76089	Aar76089 Omega con
5	151	100.0	25	2	AAW19544	Aaw19544 Natural o
6	151	100.0	25	2	AAW19569	Aaw19569 SNX-279,
7	151	100.0	25	2	AAW12967	Aaw12967 Omega con
8	151	100.0	25	2	AAW72605	Aaw72605 Conus gen
9	151	100.0	25	2	AAW95564	Aaw95564 Omega-con
10	151	100.0	25	2	AAY42335	Aay42335 Omega-con
11	151	100.0	25	3	AAY56473	Aay56473 Natural o
12	151	100.0	25	3	AAY43714	Aay43714 Amino aci
13	151	100.0	25	3	AAB14352	Aab14352 Omega-con
14	151	100.0	25	4	AAB92219	Aab92219 Toxin pep
15	151	100.0	25	4	AAB19442	Aab19442 Primary s
16	151	100.0	25	4	AAB97046	Aab97046 Omega-con
17	151	100.0	25	5	AAO15124	Aao15124 Cone snai
18	151	100.0	26	2	AAR12546	Aar12546 Omega con
19	151	100.0	26	2	AAR37765	Aar37765 SNX-193.
20	151	100.0	26	2	AAW19557	Aaw19557 SNX-193,
21	151	100.0	26	3	AAY56485	Aay56485 Analogue
22	151	100.0	27	2	AAR13266	Aar13266 Omega con
23	151	100.0	27	2	AAR13265	Aar13265 Omega con
24	151	100.0	27	2	AAR37768	Aar37768 SNX-196.
25	151	100.0	27	2	AAR37769	Aar37769 SNX-197.
26	151	100.0	27	2	AAW19561	Aaw19561 SNX-197,
27	151	100.0	27	2	AAW19560	Aaw19560 SNX-196,
28	151	100.0	27	3	AAY56488	Aay56488 Analogue
29	151	100.0	27	3	AAY56489	Aay56489 Analogue
30	151	100.0	29	3	AAY84655	Aay84655 Amino aci
31	151	100.0	32	3	AAY84656	Aay84656 Amino aci
32	151	100.0	32	3	AAY84654	Aay84654 Amino aci
33	148	98.0	25	2	AAR12547	Aar12547 Omega con
34	148	98.0	25	4	AAB97043	Aab97043 Omega-con
35	147	97.4	25	4	AAB97044	Aab97044 Omega-con
36	147	97.4	25	4	AAB97045	Aab97045 Omega-con
37	145	96.0	25	2	AAR12544	Aar12544 Omega con
38	145	96.0	25	2	AAR13264	Aar13264 Omega con
39	145	96.0	25	2	AAR12545	Aar12545 Omega con
40	145	96.0	25	2	AAR39625	Aar39625 SNX-198.
41	145	96.0	25	2	AAR39618	Aar39618 SNX-190.
42	145	96.0	25	2	AAR39621	Aar39621 SNX-194.
43	145	96.0	25	2	AAR39622	Aar39622 SNX-195.
44	145	96.0	25	2	AAR39619	Aar39619 SNX-191.
45	145	96.0	25	2	AAR39626	Aar39626 SNX-200.
46	145	96.0	25	2	AAR37763	Aar37763 SNX-190.
47	145	96.0	25	2	AAR37771	Aar37771 SNX-200.
48	145	96.0	25	2	AAR37767	Aar37767 SNX-195.
49	145	96.0	25	2	AAR37766	Aar37766 SNX-194.
50	145	96.0	25	2	AAR37764	Aar37764 SNX-191.

ALIGNMENTS

RESULT 1
AAR39608
ID AAR39608 standard; peptide; 25 AA.
XX
AC AAR39608;
XX
DT 25-MAR-2003 (revised)
DT 20-DEC-1993 (first entry)
XX
DE MVIIA/SNX111.
XX
KW Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW narcotics.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9313128-A1.
XX
PD 08-JUL-1993.
XX
PF 30-DEC-1992; 92WO-US011349.
XX
PR 30-DEC-1991; 91US-00814759.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Justice A, Singh T, Gohil K, Valentino KL, Miljanich GP;
XX
DR WPI; 1993-227270/28.
XX
PT Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT pain etc.
XX
PS Claim 1; Fig 1; 90pp; English.
XX

CC The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC derivatives of these, which may be used to produce analgesia in a mammal.
CC These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC tissue. This is shown by the peptides ability to stimulate contraction in
CC guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC neuronal tissue. OCTs are components of peptide toxins derived from
CC marine snails of the genus Conus, and act as calcium channel blockers.
CC These OCTs may be used to replace opiods in the treatment of chronic pain
CC or to reduce the opiod dosage required. This helps to reduce dependence
CC on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC PN field.)
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 2
AAR37752
ID AAR37752 standard; peptide; 25 AA.
XX
AC AAR37752;
XX
DT 25-MAR-2003 (revised)
DT 08-SEP-1993 (first entry)
XX
DE MVIIA/SNX-111.
XX
KW Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW N-channel mediated neurotransmitter release.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9310145-A1.
XX
PD 27-MAY-1993.
XX
PF 12-NOV-1992; 92WO-US009766.
XX
PR 12-NOV-1991; 91US-00789913.
PR 17-JUL-1992; 92US-00916478.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bowersox SS, Fox JA, Valentino KL, Bitner RS;
PI Yamashiro DH;
XX
DR WPI; 1993-182487/22.
XX
PT Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS Disclosure; Fig 1; 103pp; English.
XX
CC Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC damage caused by stroke. By delaying admin. for some time (compare
CC US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC in blood pressure caused by (I)). (I) is also at least as effective as
CC the specified conotoxins for (1) selective inhibition of N-type voltage-
CC gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC channel mediated neurotransmitter release in neuronal tissue. Primary
CC sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC correct PN field.)
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 3
AAR32777
ID AAR32777 standard; peptide; 25 AA.
XX
AC AAR32777;
XX
DT 28-JUN-1993 (first entry)
XX
DE MVIIA omega conotoxin peptide.
XX
KW OCT; neuronal damage reduction; ischemia; secondary damage; stroke.
XX
OS Synthetic.
XX
PN US5189020-A.
XX
PD 23-FEB-1993.
XX
PF 02-AUG-1990; 90US-00561766.
XX
PR 22-NOV-1989; 89US-00440094.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bitner RS, Bowersox SS, Fox JA, Valentino KL;
PI Yamashiro DH, Tsubokawa M;
XX
DR WPI; 1993-085564/10.
XX
PT Reducing neuronal damage due to ischaemia - involves using omega
PT conotoxin peptide or fragment.
XX
PS Disclosure; Fig 1; 32pp; English.
XX
CC The sequence is that of the MVIIA omega conotoxin (OCT) peptide which can
CC bind to an OCT binding protein, inhibit voltage-gated calcium currents
CC selectively in neuronal tissue and inhibit neuronal transmitter release
CC selectively in neuronal tissue. These properties all occur within the
CC range of those of MVIIB, GVIIA, RVIA, or pref. MVIIA and GVIA OCTs. The
CC peptide can be used in reducing or preventing both anatomical and
CC functional secondary damage related to ischemia, generally as associated
CC with stroke
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 4
AAR76089
ID AAR76089 standard; peptide; 25 AA.
XX
AC AAR76089;
XX
DT 27-AUG-2003 (revised)
DT 25-MAR-2003 (revised)
DT 02-FEB-1996 (first entry)
XX
DE Omega conotoxin MVIIA peptide.
XX
KW Omega conotoxin; marine snail; Conus; voltage-gated Ca channel blocker;
KW synaptosome; membrane; fish electric organ; mammalian brain; ischaemia;
KW binding protein; binding affinity; stroke.
XX
OS Conus.
XX
FH Key   Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site   25
FT   /note= "amidated C-terminus"
XX
PN US5424218-A.
XX
PD 13-JUN-1995.
XX
PF 04-NOV-1993; 93US-00147714.
XX
PR 22-NOV-1989; 89US-00440094.
PR 02-AUG-1990; 90US-00561766.
PR 23-MAR-1992; 92US-00855269.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Valentino KL, Bowersox SS, Bitner RS, Miljanich GP, Yamashiro DH;
PI Fox JA;
XX
DR WPI; 1995-223694/29.
XX
PT Identifying cpds. able to reduce neuronal damage caused by ischaemia - by
PT measuring their affinity to omega conotoxin MVIIA binding site and
PT ability e.g. to inhibit voltage gated calcium channels.
XX
PS Disclosure; Fig 1; 31pp; English.
XX
CC The peptides AAR76089-95 are naturally occuring omega conotoxin (OCT)
CC peptides derived from marine snails of the Conus genus. The peptide
CC sequences were used to chemically synthesise the OCT peptide fragments
CC AAR76096-R76109. The OCT peptides act as voltage-gated Ca channel
CC blockers by binding to a 210 kD protein from synaptosomal membrane
CC preparations from fish electric organ or mammalian brains. The peptides
CC and their synthesised fragments can be used to screen for compounds that
CC bind to the OCT binding protein, by displacing a high affinity labelled
CC OCT, such as MVIIA, from a synaptosomal membrane preparation. The
CC compounds should have binding affinities and activities at least equal to
CC those of the natural peptides (Ki 0.44-324 nM). The screened compounds
CC are potentially useful in treating ischaemic conditions, esp. stroke, and
CC can reduce sec. anatomical and functional damage associated with those
CC conditions. (Updated on 25-MAR-2003 to correct PF field.) (Updated on 27-
CC AUG-2003 to correct OS field.)
XX
SQ Sequence 25 AA;

```
  Query Match             100.0%;  Score 151;  DB 2;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 5
AAW19544
ID AAW19544 standard; peptide; 25 AA.
XX
AC AAW19544;
XX
DT 27-AUG-2003 (revised)
DT 13-OCT-1997 (first entry)
XX
DE Natural omega-conopeptide MVIIA/SNX-111 used for pain relief.
XX
KW Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW N-type voltage-sensitive calcium channel; block; Conus.
XX
OS Conus.
XX
FH Key   Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site   25
FT   /note= "optionally amidated"
XX
PN WO9701351-A1.
XX
PD 16-JAN-1997.
XX
PF 26-JUN-1996; 96WO-US011041.
XX
PR 27-JUN-1995; 95US-00496847.
PR 08-MAR-1996; 96US-00613400.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Amstutz GA, Bowersox SS, Gohil K, Adriaenssens PI, Kristipati R;
PI Gadbois T, Pettus MR, Luther RR;
XX
DR WPI; 1997-100012/09.
XX
PT Stable omega conopeptide compositions - for producing analgesia and for
PT inhibiting progression of neuropathic pain disorders.
XX
PS Claim 3; Fig 1, Fig 3; 47pp; English.
XX
CC AAW19544-W19553 are naturally occurring omega conopeptides (OCs) isolated
CC from Conus sp. (cone snails). The peptides and their analogues are used
CC as analgesics acting by blocking N-type voltage-sensitive calcium
CC channels. The OCs can be used to treat neuropathic pain as a result of
CC e.g. insult to the spinal cord or peripheral nerves, cancer, bone
CC degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes zoster
CC neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC hyperalgesia. The OCs are preferably administered in a medicament via an
CC epidural route in a continuous infusion or sustained release formulation.
CC The OCs can provide pain relief when administered epidurally in the
CC absence of a permeation enhancer, at doses that are comparable to
CC effective analgesic doses using intrathecal administration. OC
CC formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC They also confer stability to solutions containing them for prolonged
CC treatment methods and long-term storage. (Updated on 27-AUG-2003 to
CC correct OS field.)
XX
SQ Sequence 25 AA;

```
  Query Match             100.0%;  Score 151;  DB 2;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 6
AAW19569
ID AAW19569 standard; peptide; 25 AA.
XX
AC AAW19569;
XX
DT 14-OCT-1997 (first entry)
XX
DE SNX-279, omega conopeptide derivative used for pain relief.
XX
KW Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW N-type voltage-sensitive calcium channel; block; Conus.
XX
OS Synthetic.
XX
FH Key   Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Misc-difference 12
FT   /label= Met(O)
FT   /note= "sulphoxymethionine"
FT Disulfide-bond 15. .25
FT Modified-site   25
FT   /note= "amidated"
XX
PN WO9701351-A1.
XX
PD 16-JAN-1997.
XX
PF 26-JUN-1996; 96WO-US011041.
XX
PR 27-JUN-1995; 95US-00496847.
PR 08-MAR-1996; 96US-00613400.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Amstutz GA, Bowersox SS, Gohil K, Adriaenssens PI, Kristipati R;
PI Gadbois T, Pettus MR, Luther RR;
XX
DR WPI; 1997-100012/09.
XX
PT Stable omega conopeptide compositions - for producing analgesia and for
PT inhibiting progression of neuropathic pain disorders.
XX
PS Claim 3; Fig 3; 47pp; English.
XX
CC AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC peptides from Conus sp. (cone snails). The peptides and their analogues
CC are used as analgesics acting by blocking N-type voltage-sensitive
CC calcium channels. The OCs can be used to treat neuropathic pain as a
CC result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC hyperalgesia. The OCs are preferably administered in a medicament via an
CC epidural route in a continuous infusion or sustained release formulation.
CC The OCs can provide pain relief when administered epidurally in the
CC absence of a permeation enhancer, at doses that are comparable to
CC effective analgesic doses using intrathecal administration. OC
CC formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC They also confer stability to solutions containing them for prolonged
CC treatment methods and long-term storage
XX
SQ Sequence 25 AA;

```
  Query Match             100.0%;  Score 151;  DB 2;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 7
AAW12967
ID AAW12967 standard; peptide; 25 AA.
XX
AC AAW12967;
XX
DT 25-MAR-2003 (revised)
DT 22-APR-1997 (first entry)
XX
DE Omega conopeptide SNX-111.
XX
KW Omega conopeptide; analgesic; treatment; neuropathic pain; inhibition;
KW neuronal damage; schizophrenia; tardive dyskinesia; analgesia;
KW acute dystonic reactions; inflammation; epilepsy.
XX
OS Synthetic.
XX
PN US5587454-A.
XX
PD 24-DEC-1996.
XX
PF 15-APR-1993; 93US-00049794.
XX
PR 30-DEC-1991; 91US-00814759.
PR 30-DEC-1992; 92WO-US011349.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Gohil KC, Miljanich GP, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1997-064830/06.
XX
PT Omega cono:peptide(s) - useful as analgesics, esp. for treating
PT neuropathic pain.
XX
PS Example 1; Col 39-40; 58pp; English.
XX
CC The present peptide is an omega conopeptide, useful as an analgesic,
CC especially for treating neuropathic pain. The peptide, which can be
CC prepared by solid phase synthesis, can also be used to inhibit neuronal
CC damage and treat schizophrenia, tardive dyskinesia, acute dystonic
CC reactions, inflammation and epilepsy. In a rat paw formalin test, the
CC peptide had an ED50 of 0.011 microg in phase 1, and 0.011 microg in phase
CC 2 (by intrathecal administration). (Updated on 25-MAR-2003 to correct PF
CC field.)
XX
SQ Sequence 25 AA;

```
  Query Match             100.0%;  Score 151;  DB 2;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
```

RESULT 8
AAW72605
ID AAW72605 standard; peptide; 25 AA.
XX
AC AAW72605;
XX
DT 27-AUG-2003 (revised)
DT 06-JAN-1999 (first entry)
XX
DE Conus genus natural omega-conopeptide MVIIA/SNX-111.

XX
KW Conus genus; marine snail; cone snail; omega-conopeptide; analgesia;
KW nociceptive pain; neuropathic pain; neuronal tissue; conotoxin;
KW inflammation; schizophrenia; tardive dyskinesia; acute dystonic reaction;
KW rheumatoid arthritis; epilepsy.
XX
OS Conus.
XX
PN US5824645-A.
XX
PD 20-OCT-1998.
XX
PF 01-NOV-1996; 96US-00742774.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Valentino KL, Gohil KC, Justice A, Singh T;
XX
DR WPI; 1998-582596/49.
XX
PT Treatment of inflammation, comprises administration of omega-conopeptide
PT - effective to block voltage-gated calcium channels, bind with high
PT affinity to omega-conopeptide binding site, and inhibit neuro=transmitter
PT release.
XX
PS Disclosure; Fig 1; 58pp; English.
XX
CC A method has been developed for the treatment of inflammation in a
CC subject. The method comprises administration of an omega-conopeptide
CC effective to: (i) block voltage-gated calcium channels; (ii) bind with
CC high affinity to an omega-conopeptide binding site; and (iii) inhibit
CC neurotransmitter release from nervous tissue. The method is used to treat
CC inflammation and associated pain. The treatment can also be used to
CC produce analgesia (especially in subjects experiencing neuropathic pain);
CC and to treat schizophrenia, tardive dyskinesia and acute dystonic
CC reactions, rheumatoid arthritis, and epilepsy. The present sequence
CC represents a natural omega-conopeptide. Omega-conopeptides are components
CC of peptide toxins produced by marine snails of the genus Conus, and which
CC act as calcium channel blockers. (Updated on 27-AUG-2003 to correct OS
CC field.)
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 9
AAW95564
ID AAW95564 standard; protein; 25 AA.
XX
AC AAW95564;
XX
DT 29-MAR-1999 (first entry)
XX
DE Omega-conopeptide MVIIA/SNX-111.
XX
KW Omega-conopeptide; peptide toxin; snail; calcium channel blocker;
KW analgesia; guinea pig ileum; omega-conotoxin; pain; neuropathic.
XX
OS Synthetic.
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Modified-site 25
FT /note= "C-terminal amide"
XX
PN US5859186-A.
XX
PD 12-JAN-1999.
XX
PF 03-JUL-1996; 96US-00675354.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Gohil KC, Valentino KL, Justice A, Singh T;
XX
DR WPI; 1999-120002/10.
XX
PT Production of analgesia in mammal - by administration of omega cono-
PT peptide(s).
XX
PS Claim 3; Fig 1; 59pp; English.
XX
CC Sequences AAW95564-573 represent primary sequences of natural omega-
CC conopeptides. Omega-conopeptides are components of peptide toxins
CC produced by marine snails of the genus Conus, and which act as calcium
CC channel blockers. The invention relates to a method of producing
CC analgesia in a mammal that comprises administering an omega conopeptide
CC having activities in (a) inhibiting electrically stimulated contraction
CC of guinea pig ileum and (b) selectively binding to omega conopeptide
CC MVIIA binding sites in neuronal tissue, where these activities are within
CC the ranges of those of omega-conotoxins MVIIA and TVIA. The method is
CC used for treating chronic pain, especially neuropathic pain. The present
CC sequence is a specifically claimed example of an omega-conopeptide that
CC can be used in the method of the invention
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 10
AAY42335
ID AAY42335 standard; peptide; 25 AA.
XX
AC AAY42335;
XX
DT 20-DEC-1999 (first entry)
XX
DE Omega-conotoxin OCT MVIIA.
XX
KW Calcium channel; neuron; retina; optic nerve; trauma; ischaemia; vision;
KW prevention.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Misc-difference 25
FT /note= "Optionally contains C-terminal amide"
XX
PN US5965534-A.
XX
PD 12-OCT-1999.
XX

PF 13-MAR-1998; 98US-00039168.
XX
PR 22-NOV-1995; 95US-00562142.
XX
PA (ALCO-) ALCON LAB INC.
XX
PI Hellberg M, Pang I, Kapin M;
XX
DR WPI; 1999-579926/49.
XX
PT Treatment or prevention of retinal or optic nerve head damage comprises
PT administration of an omega-conotoxin derivative.
XX
PS Claim 2; Col 3-4; 7pp; English.
XX
CC This sequence represents omega-conotoxin OCT MVIIA. Omega-conotoxins
CC selectively block N-type calcium channels responsible for calcium influx
CC in neurons. Acute retinal or optic nerve damage, which can result in the
CC loss of vision, is caused by acute trauma and pathological events such as
CC ischaemia, hypoxia or oedema. The release of excitatory amino acids is
CC implicated in ischaemia-related neuronal and retinal damage, with
CC excitatory amino acid release leading to excessive stimulation of post-
CC synaptic excitatory amino acid receptors, which can result in cell
CC injury. The release of such excitatory amino acids from presynaptic nerve
CC terminals is dependent upon an elevation of calcium in the nerve
CC terminal. This presynaptic calcium influx is mediated by the N-type
CC calcium channels that are inhibited by omega-conotoxins. Intraocular
CC administration of at least one omega-conotoxin could be used for the
CC treatment or prevention of retinal or optic nerve head damage resulting
CC from acute traumatic or acute ischaemic events
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 2; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 11
AAY56473
ID AAY56473 standard; peptide; 25 AA.
XX
AC AAY56473;
XX
DT 16-FEB-2000 (first entry)
XX
DE Natural omega conopeptide MVIIA/SNX-111.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 1; 47pp; English.
XX
CC A method has been developed of selecting a test compound for treating
CC inflammation. The method comprises measuring the activity of the test
CC compound in blocking voltage-gated calcium channels, binding to the omega
CC conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC release from nervous tissue. The method is useful for selecting compounds
CC for treating inflammation. The selected compounds are capable of
CC producing analgesia in a mammalian subject with chronic or intractable
CC pain. Analgesia caused by selected compounds may reduce the reliance on
CC opioid analgesic agents of the prior art which cause dependency and
CC tolerance, requiring potentially dangerous increases in opioid doses to
CC achieve the analgesic effect. The present sequence represents an omega
CC conopeptide given in the present invention
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 3; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 12
AAY43714
ID AAY43714 standard; peptide; 25 AA.
XX
AC AAY43714;
XX
DT 11-FEB-2000 (first entry)
XX
DE Amino acid sequence of an omega-conotoxin MVIIA(SNX-III).
XX
KW Omega-conotoxin; venom; predatory marine snail; N-type calcium channel;
KW neuronal damage reduction; ischemia; analgesia; opiate analgesia;
KW schizophrenia; stimulant induced psychosis; hypertension; inflammation;
KW bronchotension; neuropathic pain; voltage sensitive calcium channel.
XX
OS Conus magus.
XX
PN WO9954350-A1.
XX
PD 28-OCT-1999.
XX
PF 16-APR-1999; 99WO-AU000288.
XX
PR 16-APR-1998; 98AU-00002989.
PR 01-FEB-1999; 99AU-00008419.
XX
PA (UYQU) UNIV QUEENSLAND.
XX
PI Drinkwater RD, Lewis RJ, Alewood PF, Nielsen KJ;
XX
DR WPI; 2000-013226/01.
XX
PT Novel peptides used for the treatment of disorders and diseases where
PT blockage of the N-type calcium channels is required.
XX
PS Disclosure; Page 12; 81pp; English.
XX
CC The present sequence represents an omega-conotoxin. Omega-conotoxins are
CC isolated from venoms of predatory marine snails, and have a selectivity

CC for N-type calcium channels over P/Q type channels, and so block N-type
CC calcium channels. The omega-conotoxins of the invention can be used in
CC any disease or disorder where blockage of N-type calcium channels is
CC required, e.g. in the reduction of neuronal damage following ischemia,
CC production of analgesia, or enhancement of opiate analgesia, in the
CC treatment of schizophrenia, stimulant induced psychoses, hypertension,
CC inflammation, and diseases which cause bronchotension, and also in the
CC inhibition of progression of neuropathic pain. They can also be used in a
CC screen to identify compounds with activity at N-type voltage sensitive
CC calcium channels
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 3; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 13
AAB14352
ID AAB14352 standard; peptide; 25 AA.
XX
AC AAB14352;
XX
DT 06-DEC-2000 (first entry)
XX
DE Omega-conopeptide MVIIA/SNX-111.
XX
KW Marine snail; omega-conopeptide; calcium channel blocker; MVIIA; SNX-111;
KW toxin; analgesic; antiinflammatory; anticonvulsant; neuroleptic;
KW norepinephrine release inhibitor; schizophrenia; tardive dyskinesia;
KW acute dystonic reaction; inflammation; epilepsy.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
FT Modified-site 25
FT /note= "C-terminal amide"
XX
PN US6087091-A.
XX
PD 11-JUL-2000.
XX
PF 23-APR-1999; 99US-00298017.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
PR 21-AUG-1998; 98US-00138439.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Singh T, Gohil KC, Valentino KL, Miljanich GP, Justice A;
XX
DR WPI; 2000-490177/43.
XX
PT Selecting a compound for producing analgesia involves measuring activity
PT of test compound in blocking voltage-gated calcium channels, binding to
PT omega conopeptide binding site and inhibiting norepinephrine release.
XX
PS Example 1; Fig 1; 58pp; English.
XX
CC The present sequence is an omega-conopeptide from marine snails of the
CC genus Conus. Omega-conopeptides are components of peptide toxins produced
CC by the cone snails, and which act as calcium channel blockers. Natural
CC omega-conopeptides and their derivatives may be useful for producing
CC analgesia in nociceptive and neuropathic pain. The peptides bind to omega
CC -conopeptide binding sites, which are present mainly in neuronal tissue,
CC and inhibit norepinephrine release from nervous tissue. Conopeptides such
CC as MVIIA and TVIA are effective as therapeutic agents for treating
CC neurogenic conditions such as schizophrenia, tardive dyskinesia and acute
CC dystonic reactions, inflammation and epilepsy
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 3; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 14
AAB92219
ID AAB92219 standard; peptide; 25 AA.
XX
AC AAB92219;
XX
DT 22-JUN-2001 (first entry)
XX
DE Toxin peptide SEQ ID NO:1395.
XX
KW Protection; endogenous therapeutic peptide; peptidase; conjugation;
KW blood component; modification; succinimidyl; maleimido group; amino;
KW hydroxyl; thiol; hormone; growth factor; neurotransmitter.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO200069900-A2.
XX
PD 23-NOV-2000.
XX
PF 17-MAY-2000; 2000WO-US013576.
XX
PR 17-MAY-1999; 99US-0134406P.
PR 10-SEP-1999; 99US-0153406P.
PR 15-OCT-1999; 99US-0159783P.
XX
PA (CONJ-) CONJUCHEM INC.
XX
PI Bridon DP, Ezrin AM, Milner PG, Holmes DL, Thibaudeau K;
XX
DR WPI; 2001-112059/12.
XX
PT Modifying and attaching therapeutic peptides to albumin prevents
PT peptidase degradation, useful for increasing length of in vivo activity.
XX
PS Disclosure; Page 653; 733pp; English.
XX
CC The present invention describes a modified therapeutic peptide (I)
CC comprising a therapeutically active amino acid region (III) and a
CC reactive group (II) (e.g. succinimidyl and maleimido groups) attached to
CC a less therapeutically active amino acid region (IV), which covalently
CC bonds with amino/hydroxyl/thiol groups on blood components to form a
CC peptidase stabilised therapeutic peptide composed of 3-50 amino acids.
CC (I) are useful for modifying therapeutic peptides e.g. hormones, growth
CC factors and neurotransmitters, to protect them from peptidase activity in
CC vivo for the treatment of various disorders. Endogenous therapeutic
CC peptides are not suitable as drug candidates as they require frequent
CC administration due to rapid degradation by peptidases in the body.
CC Modifying and attaching therapeutic peptides to albumin prevents or
CC reduces the action of peptidases to increase length of activity (half
CC life) and specificity as bonding to large molecules decreases
CC intracellular uptake and interference with physiological processes.
CC AAB90829 to AAB92441 represent peptides which can be used in the

```
CC   exemplification of the present invention
XX
SQ   Sequence 25 AA;

  Query Match          100.0%;  Score 151;  DB 4;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 15
AAB19442
ID   AAB19442 standard; peptide; 25 AA.
XX
AC   AAB19442;
XX
DT   06-MAR-2001  (first entry)
XX
DE   Primary sequence of a natural omega-conopeptide MVIIA/SNX-111.
XX
KW   Omega-conopeptide; voltage-gated calcium channel inhibitor; analgesic;
KW   peptide toxin; opiate; pain; neuronal damage; ischemic condition;
KW   schizophrenia; tardive dyskinesia; acute dystonic reaction; inflammation;
KW   epilepsy.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "amidated C-terminal"
XX
PN   US6136786-A.
XX
PD   24-OCT-2000.
XX
PF   09-SEP-1999;   99US-00392979.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   23-JUN-1993;   93US-00081863.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
PR   21-AUG-1998;   98US-00138439.
PR   23-APR-1999;   99US-00298017.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Singh T,  Gohil KC,  Valentino KL,  Miljanich GP,  Justice A;
XX
DR   WPI; 2001-030946/04.
XX
PT   Enhancing analgesia produced by opiates by administering an omega-
PT   conopeptide that inhibits electrically stimulated contraction of guinea
PT   pig ilium and binds to omega-conopeptide MVIIA binding sites in neuronal
PT   tissues.
XX
PS   Disclosure; Fig 1; 58pp; English.
XX
CC   The present sequence represents an omega-conopeptide. Omega-conopeptides
CC   are components of peptide toxins which act as voltage-gated calcium
CC   channel inhibitors. The peptides are used to enhance the analgesic effect
CC   produced by an opiate in a mammalian subject. The method comprises
CC   administering to the subject an omega-conopeptide which is able to
CC   inhibit electrically stimulated contraction of the guinea pig ileum and
CC   bind to omega-conopeptide MVIIA binding sites present in neuronal tissue.
CC   Omega-conopeptides are useful for enhancing the analgesic effect produced
CC   by an opiate. Omega-conopeptides may also be used in the treatment of
CC   pain, in reducing neuronal damage related to an ischemic condition in
CC   mammals, and in treating schizophrenia, tardive dyskinesia and acute
CC   dystonic reactions, inflammation and epilepsy
XX
SQ   Sequence 25 AA;

  Query Match          100.0%;  Score 151;  DB 4;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 16
AAB97046
ID   AAB97046 standard; peptide; 25 AA.
XX
AC   AAB97046;
XX
DT   20-JUL-2001  (first entry)
XX
DE   Omega-conch toxin MVIIA.
XX
KW   Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS   Unidentified.
XX
PN   CN1280136-A.
XX
PD   17-JAN-2001.
XX
PF   10-JUL-2000; 2000CN-00109828.
XX
PR   10-JUL-2000; 2000CN-00109828.
XX
PA   (LIUJ/) LIU J.
XX
PI   Liu P,  Liu J;
XX
DR   WPI; 2001-282466/30.
XX
PT   Gene sequence and amino-acid sequence of variant omega-conch toxin
PT   polypeptide, their preparation and medicinal use.
XX
PS   Disclosure; Page 10 (disclosure); 16pp; Chinese.
XX
CC   The present sequence is provided in a specification relating to gene
CC   sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC   polypeptides. The polypeptides may be used for treating pain and nerve
CC   cell damage. The methionine at position 12 of natural Omega-conch toxin
CC   is changed into alanine, glycine, isoleucine or valine. The genes
CC   encoding the Omega-conch toxin and its variant polypeptides are connected
CC   serially into a polymer, and the Omega-conch toxin polymer is prepared
CC   using a prokaryotic or eukaryotic expression system
XX
SQ   Sequence 25 AA;

  Query Match          100.0%;  Score 151;  DB 4;  Length 25;
  Best Local Similarity   100.0%;  Pred. No. 3.7e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 17
AAO15124
ID   AAO15124 standard; peptide; 25 AA.
XX
AC   AAO15124;
```

XX
DT 22-AUG-2002 (first entry)
XX
DE Cone snail w-conotoxin peptide MVIIA.
XX
KW Cone snail; venomous saliva; calcium channel blocking activity;
KW stenocardia; hypertension; myocarditis; arrhythmia; cerebral ischaemia;
KW w-conotoxin.
XX
OS Conus sp.
XX
PN JP2002080499-A.
XX
PD 19-MAR-2002.
XX
PF 01-SEP-2000; 2000JP-00266187.
XX
PR 01-SEP-2000; 2000JP-00266187.
XX
PA (SUNR) SUNTORY LTD.
XX
DR WPI; 2002-421068/45.
XX
PT A new peptide derived from venomous saliva of assassin bug, has calcium
PT channel blocking activity.
XX
PS Disclosure; Page 4; 26pp; Japanese.
XX
CC The invention comprises peptides having calcium channel blocking
CC activities which are derived from the venomous saliva of assassin bugs.
CC The calcium channel blocking peptides of the invention are useful for
CC treating stenocardia, hypertension, myocarditis, arrhythmia and cerebral
CC ischaemia. The present amino acid sequence represents a cone snail w-
CC conotoxin peptide
XX
SQ Sequence 25 AA;

Query Match 100.0%; Score 151; DB 5; Length 25;
Best Local Similarity 100.0%; Pred. No. 3.7e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 18
AAR12546
ID AAR12546 standard; protein; 26 AA.
XX
AC AAR12546;
XX
DT 05-SEP-1991 (first entry)
XX
DE Omega conotoxin peptide analogue MVIIA(193).
XX
KW neuronal calcium-channel antagonist; OCT; adrenaline release;
KW neuroprotective.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9107980-A.
XX
PD 13-JUN-1991.
XX
PF 22-NOV-1989; 89US-00440094.
XX
PR 22-NOV-1989; 89US-00440094.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanjich GP, Bitner RS, Bowersox SS, Fox JA, Valentino KL;
PI Yamashiro DH;
XX
DR WPI; 1991-192969/26.
XX
PT Compsn. for reducing ischaemia-related neuronal damage - contains
PT neuronal channel antagonist omega conotoxin peptide which blocks
PT norepinephrine release in central nervous system neuronal cells.
XX
PS Disclosure; Fig 2; 74pp; English.
XX
CC MVIIA(193) is an analogue of OCT peptide MVIIA in which a Gly residue is
CC added to the C-terminus. The analogue gave IC(50) for inhibition of
CC adrenaline release and Ki values within the ranges of those of OCT
CC peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC neuroprotective compound. See also AAR12542-5, AAR12547 and AAR13264-6
XX
SQ Sequence 26 AA;

Query Match 100.0%; Score 151; DB 2; Length 26;
Best Local Similarity 100.0%; Pred. No. 3.8e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 19
AAR37765
ID AAR37765 standard; peptide; 26 AA.
XX
AC AAR37765;
XX
DT 25-MAR-2003 (revised)
DT 08-SEP-1993 (first entry)
XX
DE SNX-193.
XX
KW Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW N-channel mediated neurotransmitter release.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9310145-A1.
XX
PD 27-MAY-1993.
XX
PF 12-NOV-1992; 92WO-US009766.
XX
PR 12-NOV-1991; 91US-00789913.
PR 17-JUL-1992; 92US-00916478.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Miljanich GP, Bowersox SS, Fox JA, Valentino KL, Bitner RS;
PI Yamashiro DH;
XX
DR WPI; 1993-182487/22.
XX
PT Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT bind specifically to omega-conotoxin MVIIA binding sites.
XX

PS Disclosure; Fig 2; 103pp; English.
XX
CC Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC damage caused by stroke. By delaying admin. for some time (compare
CC US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC in blood pressure caused by (I)). (I) is also at least as effective as
CC the specified conotoxins for (1) selective inhibition of N-type voltage-
CC gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC channel mediated neurotransmitter release in neuronal tissue. Primary
CC sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC correct PN field.)
XX
SQ Sequence 26 AA;

Query Match 100.0%; Score 151; DB 2; Length 26;
Best Local Similarity 100.0%; Pred. No. 3.8e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 20
AAW19557
ID AAW19557 standard; peptide; 26 AA.
XX
AC AAW19557;
XX
DT 14-OCT-1997 (first entry)
XX
DE SNX-193, omega conopeptide derivative used for pain relief.
XX
KW Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW N-type voltage-sensitive calcium channel; block; Conus.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN WO9701351-A1.
XX
PD 16-JAN-1997.
XX
PF 26-JUN-1996; 96WO-US011041.
XX
PR 27-JUN-1995; 95US-00496847.
PR 08-MAR-1996; 96US-00613400.
XX
PA (NEUR-) NEUREX CORP.
XX
PI Amstutz GA, Bowersox SS, Gohil K, Adriaenssens PI, Kristipati R;
PI Gadbois T, Pettus MR, Luther RR;
XX
DR WPI; 1997-100012/09.
XX
PT Stable omega conopeptide compositions - for producing analgesia and for
PT inhibiting progression of neuropathic pain disorders.
XX
PS Disclosure; Fig 3; 47pp; English.
XX
CC AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC peptides from Conus sp. (cone snails). The peptides and their analogues
CC are used as analgesics acting by blocking N-type voltage-sensitive
CC calcium channels. The OCs can be used to treat neuropathic pain as a
CC result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC hyperalgesia. The OCs are preferably administered in a medicament via an
CC epidural route in a continuous infusion or sustained release formulation.
CC The OCs can provide pain relief when administered epidurally in the
CC absence of a permeation enhancer, at doses that are comparable to
CC effective analgesic doses using intrathecal administration. OC
CC formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC They also confer stability to solutions containing them for prolonged
CC treatment methods and long-term storage
XX
SQ Sequence 26 AA;

Query Match 100.0%; Score 151; DB 2; Length 26;
Best Local Similarity 100.0%; Pred. No. 3.8e-10;
Matches 25; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||||||||||||||||||
Db 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25

RESULT 21
AAY56485
ID AAY56485 standard; peptide; 26 AA.
XX
AC AAY56485;
XX
DT 16-FEB-2000 (first entry)
XX
DE Analogue omega conopeptide SNX-193.
XX
KW Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW marine snail; peptide toxin; inflammation; binding;
KW voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW anti-inflammatory.
XX
OS Conus sp.
XX
FH Key Location/Qualifiers
FT Disulfide-bond 1. .16
FT Disulfide-bond 8. .20
FT Disulfide-bond 15. .25
XX
PN US5994305-A.
XX
PD 30-NOV-1999.
XX
PF 21-AUG-1998; 98US-00138439.
XX
PR 30-DEC-1991; 91US-00814759.
PR 15-APR-1993; 93US-00049794.
PR 03-JUL-1996; 96US-00675354.
PR 01-NOV-1996; 96US-00742774.
XX
PA (ELAN-) ELAN PHARM INC.
XX
PI Justice A, Singh T, Valentino KL, Miljanich GP, Gohil KC;
XX
DR WPI; 2000-038270/03.
XX
PT Measuring the activity of test compounds in blocking voltage-gated
PT calcium channels, binding to the omega conopeptide binding site and
PT inhibiting norepinephrine (noradrenaline) release for treating
PT inflammation.
XX
PS Disclosure; Fig 2; 47pp; English.
XX

```
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 26 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 26;
  Best Local Similarity   100.0%;  Pred. No. 3.8e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 22
AAR13266
ID   AAR13266 standard; protein; 27 AA.
XX
AC   AAR13266;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(197).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(197) is an analogue of OCT peptide MVIIA in which an Asn-Ser
CC   dipeptide has been added to the N-terminus. residue replaces Lys at
CC   position 2. The analogue gave IC(50) for inhibition of adrenaline release
CC   and Ki values outside the ranges of those of OCT peptides MVIIA, GVIA,
CC   and/or TVIA. It is thus not a candidate for a neuroprotective compound.
CC   See also AAR12542-7, AAR13264-5
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 23
AAR13265
ID   AAR13265 standard; protein; 27 AA.
XX
AC   AAR13265;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(196).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(196) is an analogue of OCT peptide MVIIA in which an Asn residue is
CC   addede to the N-terminus and a Gly residue is added to the C-terminus.
CC   The analogue gave IC(50) for inhibition of adrenaline release and Ki
CC   values within the ranges of those of OCT peptides MVIIA, GVIA, and/or
CC   TVIA. It is thus a candidate for a neuroprotective compound. See also
CC   AAR12542-7, AAR13264 and AAR13266
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 24
AAR37768
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ID   AAR37768 standard; peptide; 27 AA.
XX
AC   AAR37768;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-196.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   Ischaemia-related neuronal damage in mammals is reduced by admin., 4-24
CC   hr after onset of ischaemia, of a cpd. (I) which binds selectively to an
CC   omega-conotoxin (OCT) MVIIA site in neuronal tissue. (I) has selectivity
CC   at least 100 expressed as ratio of binding affinity for the MVIIA site to
CC   that for the MVIIC site. (I) is one of the OCTs MVIIA, MVIIB, GVIA, GVIIA
CC   or RVIA or it is the cpd. SNX-207. (I) is esp. used to reduce neuronal
CC   damage caused by stroke. By delaying admin. for some time (compare
CC   US5051403 where cpds. are given within 1 hr of the onset of ischaemia) a
CC   greater redn. in neuronal damage is achieved. (I) is admin. e.g. by
CC   intracerebroventricular (ICV) injection at 0.1-20 microg/kg, but can also
CC   be given i.v. (opt. after treatment with antihistamines to minimise redn.
CC   in blood pressure caused by (I)). (I) is also at least as effective as
CC   the specified conotoxins for (1) selective inhibition of N-type voltage-
CC   gated Ca currents in neuronal tissue and (2) selective inhibition of N-
CC   channel mediated neurotransmitter release in neuronal tissue. Primary
CC   sequences of omega-conopeptides are given in AAR37752-62. Several analog
CC   omega-conopeptides are given in AAR37763-76. (Updated on 25-MAR-2003 to
CC   correct PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 25
AAR37769
ID   AAR37769 standard; peptide; 27 AA.
XX
AC   AAR37769;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-197.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27
```

```
RESULT 26
AAW19561
ID   AAW19561 standard; peptide; 27 AA.
XX
AC   AAW19561;
XX
DT   14-OCT-1997  (first entry)
XX
DE   SNX-197, omega conopeptide derivative used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Disclosure; Fig 3; 47pp; English.
XX
CC   AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC   peptides from Conus sp. (cone snails). The peptides and their analogues
CC   are used as analgesics acting by blocking N-type voltage-sensitive
CC   calcium channels. The OCs can be used to treat neuropathic pain as a
CC   result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC   bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC   zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 27
AAW19560
ID   AAW19560 standard; peptide; 27 AA.
XX
AC   AAW19560;
XX
DT   14-OCT-1997  (first entry)
XX
DE   SNX-196, omega conopeptide derivative used for pain relief.
XX
KW   Conopeptide; cone snail; pain; analgesic; neuropathy; epidural;
KW   N-type voltage-sensitive calcium channel; block; Conus.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   WO9701351-A1.
XX
PD   16-JAN-1997.
XX
PF   26-JUN-1996;   96WO-US011041.
XX
PR   27-JUN-1995;   95US-00496847.
PR   08-MAR-1996;   96US-00613400.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Amstutz GA,  Bowersox SS,  Gohil K,  Adriaenssens PI,  Kristipati R;
PI   Gadbois T,  Pettus MR,  Luther RR;
XX
DR   WPI; 1997-100012/09.
XX
PT   Stable omega conopeptide compositions - for producing analgesia and for
PT   inhibiting progression of neuropathic pain disorders.
XX
PS   Disclosure; Fig 3; 47pp; English.
XX
CC   AAW19555-W19572 are omega conopeptides (OCs) derived from natural
CC   peptides from Conus sp. (cone snails). The peptides and their analogues
CC   are used as analgesics acting by blocking N-type voltage-sensitive
CC   calcium channels. The OCs can be used to treat neuropathic pain as a
CC   result of e.g. insult to the spinal cord or peripheral nerves, cancer,
CC   bone degenerative diseases, AIDS, reflex sympathetic dystrophy, herpes
CC   zoster neuropathy, diabetic neuropathy, hyperesthesia, allodynia or
CC   hyperalgesia. The OCs are preferably administered in a medicament via an
CC   epidural route in a continuous infusion or sustained release formulation.
CC   The OCs can provide pain relief when administered epidurally in the
CC   absence of a permeation enhancer, at doses that are comparable to
CC   effective analgesic doses using intrathecal administration. OC
CC   formulations comprising an OC and a carboxylic acid buffer anti-oxidant.
CC   They also confer stability to solutions containing them for prolonged
CC   treatment methods and long-term storage
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 2;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 28
AAY56488
ID   AAY56488 standard; peptide; 27 AA.
XX
AC   AAY56488;
XX
DT   16-FEB-2000  (first entry)
XX
```

```
DE   Analogue omega conopeptide SNX-196.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  2. .17
FT   Disulfide-bond  9. .21
FT   Disulfide-bond  16. .26
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
PT   inflammation.
XX
PS   Disclosure; Fig 2; 47pp; English.
XX
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          2 CKGKGAKCSRLMYDCCTGSCRSGKC 26


RESULT 29
AAY56489
ID   AAY56489 standard; peptide; 27 AA.
XX
AC   AAY56489;
XX
DT   16-FEB-2000  (first entry)
XX
DE   Analogue omega conopeptide SNX-197.
XX
KW   Omega conopeptide; analgesic; nociceptive; neuropathic; pain; conotoxin;
KW   marine snail; peptide toxin; inflammation; binding;
KW   voltage-gated calcium channel; inhibition; norepinephrine; noradrenaline;
KW   anti-inflammatory.
XX
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  3. .18
FT   Disulfide-bond  10. .22
FT   Disulfide-bond  17. .27
FT   Modified-site   27
FT                   /note= "amidated"
XX
PN   US5994305-A.
XX
PD   30-NOV-1999.
XX
PF   21-AUG-1998;   98US-00138439.
XX
PR   30-DEC-1991;   91US-00814759.
PR   15-APR-1993;   93US-00049794.
PR   03-JUL-1996;   96US-00675354.
PR   01-NOV-1996;   96US-00742774.
XX
PA   (ELAN-) ELAN PHARM INC.
XX
PI   Justice A,  Singh T,  Valentino KL,  Miljanich GP,  Gohil KC;
XX
DR   WPI; 2000-038270/03.
XX
PT   Measuring the activity of test compounds in blocking voltage-gated
PT   calcium channels, binding to the omega conopeptide binding site and
PT   inhibiting norepinephrine (noradrenaline) release for treating
PT   inflammation.
XX
PS   Disclosure; Fig 2; 47pp; English.
XX
CC   A method has been developed of selecting a test compound for treating
CC   inflammation. The method comprises measuring the activity of the test
CC   compound in blocking voltage-gated calcium channels, binding to the omega
CC   conopeptide binding site and inhibiting norepinephrine (noradrenaline)
CC   release from nervous tissue. The method is useful for selecting compounds
CC   for treating inflammation. The selected compounds are capable of
CC   producing analgesia in a mammalian subject with chronic or intractable
CC   pain. Analgesia caused by selected compounds may reduce the reliance on
CC   opioid analgesic agents of the prior art which cause dependency and
CC   tolerance, requiring potentially dangerous increases in opioid doses to
CC   achieve the analgesic effect. The present sequence represents an omega
CC   conopeptide given in the present invention
XX
SQ   Sequence 27 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 27;
  Best Local Similarity   100.0%;  Pred. No. 3.9e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          3 CKGKGAKCSRLMYDCCTGSCRSGKC 27


RESULT 30
AAY84655
ID   AAY84655 standard; peptide; 29 AA.
XX
AC   AAY84655;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
```

```
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 1. .29
FT                   /note= "peptide is cyclised via these residues"
FT   Peptide         1. .25
FT                   /note= "conotoxin"
FT   Peptide         26. .29
FT                   /note= "linker"
XX
PN   WO200015654-A1.
XX
PD   23-MAR-2000.
XX
PF   14-SEP-1999;   99WO-AU000769.
XX
PR   14-SEP-1998;   98AU-00005895.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Craik DJ,  Daly NL,  Nielsen KJ;
XX
DR   WPI; 2000-271376/23.
XX
PT   Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT   diseases in humans.
XX
PS   Claim 10; Page 31; 43pp; English.
XX
CC   AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC   cyclised peptides have improved properties, compared to their linear
CC   counterparts. These include resistance to cleavage by proteases, high
CC   chemical stability, improved biophysical properties, reduced side effects
CC   and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC   type calcium channels, and so may be useful in the treatment of
CC   neurological disorders such as acute and chronic pain, stroke, traumatic
CC   brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC   disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC   useful in the treatment of neuropsychiatric disorders such as
CC   schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC   syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC   to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC   can be also used as neuropharmacological probes. Antibodies raised
CC   against the peptides are useful as therapeutic or diagnostic agents, and
CC   can be used to screen for the peptides
XX
SQ   Sequence 29 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 29;
  Best Local Similarity   100.0%;  Pred. No. 4.2e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 31
AAY84656
ID   AAY84656 standard; peptide; 32 AA.
XX
AC   AAY84656;
XX
DT   25-JUL-2000  (first entry)
XX
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 1. .32
FT                   /note= "peptide is cyclised via these residues"
FT   Peptide         1. .4
FT                   /note= "linker"
FT   Peptide         5. .29
FT                   /note= "conotoxin"
FT   Peptide         30. .32
FT                   /note= "linker"
XX
PN   WO200015654-A1.
XX
PD   23-MAR-2000.
XX
PF   14-SEP-1999;   99WO-AU000769.
XX
PR   14-SEP-1998;   98AU-00005895.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Craik DJ,  Daly NL,  Nielsen KJ;
XX
DR   WPI; 2000-271376/23.
XX
PT   Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT   diseases in humans.
XX
PS   Claim 10; Page 31; 43pp; English.
XX
CC   AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC   cyclised peptides have improved properties, compared to their linear
CC   counterparts. These include resistance to cleavage by proteases, high
CC   chemical stability, improved biophysical properties, reduced side effects
CC   and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC   type calcium channels, and so may be useful in the treatment of
CC   neurological disorders such as acute and chronic pain, stroke, traumatic
CC   brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC   disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC   useful in the treatment of neuropsychiatric disorders such as
CC   schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC   syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC   to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC   can be also used as neuropharmacological probes. Antibodies raised
CC   against the peptides are useful as therapeutic or diagnostic agents, and
CC   can be used to screen for the peptides
XX
SQ   Sequence 32 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 32;
  Best Local Similarity   100.0%;  Pred. No. 4.5e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          5 CKGKGAKCSRLMYDCCTGSCRSGKC 29


RESULT 32
AAY84654
ID   AAY84654 standard; peptide; 32 AA.
XX
AC   AAY84654;
XX
DT   25-JUL-2000  (first entry)
XX
```

```
DE   Amino acid sequence of a cyclised conotoxin peptide.
XX
KW   Cyclised conotoxin; omega-conotoxin; neurological disorder; pain; stroke;
KW   traumatic brain injury; migraine; epilepsy; Parkinson's disease;
KW   Alzheimer's disease; multiple sclerosis; depression; alpha-conotoxin;
KW   neuropsychiatric disorder; schizophrenia; Tourette's syndrome;
KW   mu-conotoxin.
XX
OS   Synthetic.
OS   Conus sp.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 1. .32
FT                   /note= "peptide is cyclised via these residues"
FT   Peptide         1. .26
FT                   /note= "conotoxin"
FT   Peptide         26. .32
FT                   /note= "linker"
XX
PN   WO200015654-A1.
XX
PD   23-MAR-2000.
XX
PF   14-SEP-1999;   99WO-AU000769.
XX
PR   14-SEP-1998;   98AU-00005895.
XX
PA   (UYQU ) UNIV QUEENSLAND.
XX
PI   Craik DJ,  Daly NL,  Nielsen KJ;
XX
DR   WPI; 2000-271376/23.
XX
PT   Novel cyclized conotoxin peptides useful in the therapeutic treatment of
PT   diseases in humans.
XX
PS   Claim 10; Page 31; 43pp; English.
XX
CC   AAY84654-58 represent cyclised conotoxin peptides of the ivnention. The
CC   cyclised peptides have improved properties, compared to their linear
CC   counterparts. These include resistance to cleavage by proteases, high
CC   chemical stability, improved biophysical properties, reduced side effects
CC   and improved bioavaliability. Cyclised omega-conotoxin peptides block N-
CC   type calcium channels, and so may be useful in the treatment of
CC   neurological disorders such as acute and chronic pain, stroke, traumatic
CC   brain injury, migraine, epilepsy, Parkinson's disease, Alzheimer's
CC   disease, multiple sclerosis, and depression. Alpha-conotoxins may be
CC   useful in the treatment of neuropsychiatric disorders such as
CC   schizophrenia, Parkinson's disease, Alzheimer's disease and Tourette's
CC   syndrome. Mu-conotoxins interact with neuronal channels and may be used
CC   to treat chronic and neuropathic pain. The cyclised conotoxin peptides
CC   can be also used as neuropharmacological probes. Antibodies raised
CC   against the peptides are useful as therapeutic or diagnostic agents, and
CC   can be used to screen for the peptides
XX
SQ   Sequence 32 AA;

  Query Match             100.0%;  Score 151;  DB 3;  Length 32;
  Best Local Similarity   100.0%;  Pred. No. 4.5e-10;
  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||||
Db          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 33
AAR12547
ID   AAR12547 standard; protein; 25 AA.
XX
AC   AAR12547;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(194).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Misc-difference 12
FT                   /label= Nle
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(194) is an analogue of OCT peptide MVIIA in which a Nle residue
CC   replaces Met at position 12. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-6 and AAR13264-6
XX
SQ   Sequence 25 AA;

  Query Match             98.0%;  Score 148;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 8e-10;
  Matches   24;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              ||||||||||:||||||||||||||
Db          1 CKGKGAKCSRLLYDCCTGSCRSGKC 25


RESULT 34
AAB97043
ID   AAB97043 standard; peptide; 25 AA.
XX
AC   AAB97043;
XX
DT   20-JUL-2001  (first entry)
XX
DE   Omega-conch toxin MVIIA variant polypeptide #3.
XX
KW   Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS   Unidentified.
XX
PN   CN1280136-A.
XX
PD   17-JAN-2001.
XX
```

PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 3; Page 1 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 98.0%; Score 148; DB 4; Length 25;
Best Local Similarity 96.0%; Pred. No. 8e-10;
Matches 24; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||:||||||||||||
Db 1 CKGKGAKCSRLLYDCCTGSCRSGKC 25

RESULT 35
AAB97044
ID AAB97044 standard; peptide; 25 AA.
XX
AC AAB97044;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA variant polypeptide #4.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 4; Page 1 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 97.4%; Score 147; DB 4; Length 25;
Best Local Similarity 96.0%; Pred. No. 1e-09;
Matches 24; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||:||||||||||||
Db 1 CKGKGAKCSRLIYDCCTGSCRSGKC 25

RESULT 36
AAB97045
ID AAB97045 standard; peptide; 25 AA.
XX
AC AAB97045;
XX
DT 20-JUL-2001 (first entry)
XX
DE Omega-conch toxin MVIIA variant polypeptide #5.
XX
KW Omega-conch; toxin; MVIIA; variant; pain; nerve cell damage.
XX
OS Unidentified.
XX
PN CN1280136-A.
XX
PD 17-JAN-2001.
XX
PF 10-JUL-2000; 2000CN-00109828.
XX
PR 10-JUL-2000; 2000CN-00109828.
XX
PA (LIUJ/) LIU J.
XX
PI Liu P, Liu J;
XX
DR WPI; 2001-282466/30.
XX
PT Gene sequence and amino-acid sequence of variant omega-conch toxin
PT polypeptide, their preparation and medicinal use.
XX
PS Claim 5; Page 2 (claims); 16pp; Chinese.
XX
CC The present sequence is provided in a specification relating to gene
CC sequences and amino acid sequences of Omega-conch toxin (MVIIA) variant
CC polypeptides. The polypeptides may be used for treating pain and nerve
CC cell damage. The methionine at position 12 of natural Omega-conch toxin
CC is changed into alanine, glycine, isoleucine or valine. The genes
CC encoding the Omega-conch toxin and its variant polypeptides are connected
CC serially into a polymer, and the Omega-conch toxin polymer is prepared
CC using a prokaryotic or eukaryotic expression system
XX
SQ Sequence 25 AA;

Query Match 97.4%; Score 147; DB 4; Length 25;
Best Local Similarity 96.0%; Pred. No. 1e-09;
Matches 24; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
||||||||||:||||||||||||
Db 1 CKGKGAKCSRLVYDCCTGSCRSGKC 25

RESULT 37
AAR12544
ID AAR12544 standard; protein; 25 AA.
XX
AC AAR12544;

```
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(190).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(190) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 4. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-3, AAR12545-7 and AAR13264-6
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              ||| |||||||||||||||||||||
Db          1 CKGAGAKCSRLMYDCCTGSCRSGKC 25


RESULT 38
AAR13264
ID   AAR13264 standard; protein; 25 AA.
XX
AC   AAR13264;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(195).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(195) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 24. The analogue gave a Ki value within the
CC   ranges of those of OCT peptides MVIIA, GVIA, and/or TVIA. It gave an
CC   IC(50) for inhibition of adrenaline release outside the range for these
CC   neuroprotective compounds. See also AAR12542-7, and AAR13265-6
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              ||||||||||||||||||||||| |
Db          1 CKGKGAKCSRLMYDCCTGSCRSGAC 25


RESULT 39
AAR12545
ID   AAR12545 standard; protein; 25 AA.
XX
AC   AAR12545;
XX
DT   05-SEP-1991  (first entry)
XX
DE   Omega conotoxin peptide analogue MVIIA(191).
XX
KW   neuronal calcium-channel antagonist; OCT; adrenaline release;
KW   neuroprotective.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /label= amidated carboxy terminal
XX
PN   WO9107980-A.
XX
PD   13-JUN-1991.
XX
PF   22-NOV-1989;   89US-00440094.
XX
PR   22-NOV-1989;   89US-00440094.
XX
PA   (NEUR-) NEUREX CORP.
```

```
XX
PI   Miljanjich GP,  Bitner RS,  Bowersox SS,  Fox JA,  Valentino KL;
PI   Yamashiro DH;
XX
DR   WPI; 1991-192969/26.
XX
PT   Compsn. for reducing ischaemia-related neuronal damage - contains
PT   neuronal channel antagonist omega conotoxin peptide which blocks
PT   norepinephrine release in central nervous system neuronal cells.
XX
PS   Disclosure; Fig 2; 74pp; English.
XX
CC   MVIIA(191) is an analogue of OCT peptide MVIIA in which an Ala residue
CC   replaces Lys at position 2. The analogue gave IC(50) for inhibition of
CC   adrenaline release and Ki values within the ranges of those of OCT
CC   peptides MVIIA, GVIA, and/or TVIA. It is thus a candidate for a
CC   neuroprotective compound. See also AAR12542-4, AAR12546-7 and AAR13264-6
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              | ||||||||||||||||||||||||
Db          1 CAGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 40
AAR39625
ID   AAR39625 standard; peptide; 25 AA.
XX
AC   AAR39625;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-198.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||| ||||
Db          1 CKGKGAKCSRLMYDCCTGSCASGKC 25


RESULT 41
AAR39618
ID   AAR39618 standard; peptide; 25 AA.
XX
AC   AAR39618;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-190.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
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```
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              ||| |||||||||||||||||||||
Db          1 CKGAGAKCSRLMYDCCTGSCRSGKC 25


RESULT 42
AAR39621
ID   AAR39621 standard; peptide; 25 AA.
XX
AC   AAR39621;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-194.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Modified-site   12
FT                   /label= NLE
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||| ||||||||||||
Db          1 CKGKGAKCSRLXYDCCTGSCRSGKC 25


RESULT 43
AAR39622
ID   AAR39622 standard; peptide; 25 AA.
XX
AC   AAR39622;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-195.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
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```
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||| |
Db          1 CKGKGAKCSRLMYDCCTGSCRSGAC 25


RESULT 44
AAR39619
ID   AAR39619 standard; peptide; 25 AA.
XX
AC   AAR39619;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-191.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              | |||||||||||||||||||||||
Db          1 CAGKGAKCSRLMYDCCTGSCRSGKC 25


RESULT 45
AAR39626
ID   AAR39626 standard; peptide; 25 AA.
XX
AC   AAR39626;
XX
DT   25-MAR-2003  (revised)
DT   20-DEC-1993  (first entry)
XX
DE   SNX-200.
XX
KW   Omega conopeptide; OCT; analgesia; inhibition; voltage-gated;
KW   calcium channel; neurone; contraction; guinea pig; ileum; MVIIA;
KW   binding site; toxin; marine; snail; Conus; opiod; chronic pain;
KW   narcotics.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
FT   Modified-site   25
FT                   /note= "Amidated C-terminal"
XX
PN   WO9313128-A1.
XX
PD   08-JUL-1993.
XX
PF   30-DEC-1992;   92WO-US011349.
XX
PR   30-DEC-1991;   91US-00814759.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Justice A,  Singh T,  Gohil K,  Valentino KL,  Miljanich GP;
XX
DR   WPI; 1993-227270/28.
XX
PT   Use of omega-cono-peptide(s) which selectively inhibit voltage-gated
PT   calcium channels - to induce analgesia, enhance opiate analgesics, treat
PT   pain etc.
XX
PS   Claim 1; Fig 2; 90pp; English.
XX
CC   The sequences given in AAR39608-30 are omega conopeptides (OCTs) and
CC   derivatives of these, which may be used to produce analgesia in a mammal.
CC   These OCTs inhibit voltage-gated calcium channels selectively in neuronal
CC   tissue. This is shown by the peptides ability to stimulate contraction in
CC   guinea pig ileum and to bind to OCT MVIIA binding sites present in
CC   neuronal tissue. OCTs are components of peptide toxins derived from
CC   marine snails of the genus Conus, and act as calcium channel blockers.
CC   These OCTs may be used to replace opiods in the treatment of chronic pain
CC   or to reduce the opiod dosage required. This helps to reduce dependence
CC   on and tolerance to opiod narcotics. (Updated on 25-MAR-2003 to correct
CC   PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||| ||||||||||||||||||
Db          1 CKGKGAACSRLMYDCCTGSCRSGKC 25
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RESULT 46
AAR37763
ID   AAR37763 standard; peptide; 25 AA.
XX
AC   AAR37763;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-190.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              ||| ||||||||||||||||||||||
Db          1 CKGAGAKCSRLMYDCCTGSCRSGKC 25
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RESULT 47
AAR37771
ID   AAR37771 standard; peptide; 25 AA.
XX
AC   AAR37771;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-200.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
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Db          1 CKGKGAACSRLMYDCCTGSCRSGKC 25


RESULT 48
AAR37767
ID   AAR37767 standard; peptide; 25 AA.
XX
AC   AAR37767;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-195.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||||||||||||||| |
Db          1 CKGKGAKCSRLMYDCCTGSCRSGAC 25


RESULT 49
AAR37766
ID   AAR37766 standard; peptide; 25 AA.
XX
AC   AAR37766;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-194.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Modified-site   12
FT                   /label= NLE
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
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  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              |||||||||||  ||||||||||||
Db          1 CKGKGAKCSRLXYDCCTGSCRSGKC 25


RESULT 50
AAR37764
ID   AAR37764 standard; peptide; 25 AA.
XX
AC   AAR37764;
XX
DT   25-MAR-2003  (revised)
DT   08-SEP-1993  (first entry)
XX
DE   SNX-191.
XX
KW   Ischaemia; neuronal; omega-conotoxin; OCT; MVIIA; MVIIC; MVIID; MVIIB;
KW   GVIA; GVIIA; RVIA; SVIA; TVIA; SVIB; SNX-207; stroke; delayed treatment;
KW   antihistamine; blood pressure; N-type voltage-gated Ca currents;
KW   N-channel mediated neurotransmitter release.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Disulfide-bond  1. .16
FT   Disulfide-bond  8. .20
FT   Disulfide-bond  15. .25
XX
PN   WO9310145-A1.
XX
PD   27-MAY-1993.
XX
PF   12-NOV-1992;   92WO-US009766.
XX
PR   12-NOV-1991;   91US-00789913.
PR   17-JUL-1992;   92US-00916478.
XX
PA   (NEUR-) NEUREX CORP.
XX
PI   Miljanich GP,  Bowersox SS,  Fox JA,  Valentino KL,  Bitner RS;
PI   Yamashiro DH;
XX
DR   WPI; 1993-182487/22.
XX
PT   Redn. of neuronal damage caused by ischaemia - by admin. of cpds. that
PT   bind specifically to omega-conotoxin MVIIA binding sites.
XX
PS   Disclosure; Fig 2; 103pp; English.
XX
CC   The C-terminal is amidated. Ischaemia-related neuronal damage in mammals
CC   is reduced by admin., 4-24 hr after onset of ischaemia, of a cpd. (I)
CC   which binds selectively to an omega-conotoxin (OCT) MVIIA site in
CC   neuronal tissue. (I) has selectivity at least 100 expressed as ratio of
CC   binding affinity for the MVIIA site to that for the MVIIC site. (I) is
CC   one of the OCTs MVIIA, MVIIB, GVIA, GVIIA or RVIA or it is the cpd. SNX-
CC   207. (I) is esp. used to reduce neuronal damage caused by stroke. By
CC   delaying admin. for some time (compare US5051403 where cpds. are given
CC   within 1 hr of the onset of ischaemia) a greater redn. in neuronal damage
CC   is achieved. (I) is admin. e.g. by intracerebroventricular (ICV)
CC   injection at 0.1-20 microg/kg, but can also be given i.v. (opt. after
CC   treatment with antihistamines to minimise redn. in blood pressure caused
CC   by (I)). (I) is also at least as effective as the specified conotoxins
CC   for (1) selective inhibition of N-type voltage-gated Ca currents in
CC   neuronal tissue and (2) selective inhibition of N-channel mediated
CC   neurotransmitter release in neuronal tissue. Primary sequences of omega-
CC   conopeptides are given in AAR37752-62. Several analog omega-conopeptides
CC   are given in AAR37763-76. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 25 AA;

  Query Match             96.0%;  Score 145;  DB 2;  Length 25;
  Best Local Similarity   96.0%;  Pred. No. 1.7e-09;
  Matches   24;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 CKGKGAKCSRLMYDCCTGSCRSGKC 25
              | ||||||||||||||||||||||||
Db          1 CAGKGAKCSRLMYDCCTGSCRSGKC 25


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Job time : 67.6667 secs
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